THE PHILIPPINE
JOURNAL OF SCIENCE

EDITED BY

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PUBLISHED BY

THE BUREAU OF SCIENCE

OF THE

GOVERNMENT OF THE PHILIPPINE ISLANDS

B. MEDICAL SCIENCES

VOLUME V

1910

WITH 34 PLATES, 5 FIGURES, 11 CHARTS AND 1 DIAGRAM

MANILA
BUREAU OF PRINTING
1910
99967

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THE PHILIPPINE
JOURNAL OF SCIENCE
B. MEDICAL SCIENCES

VOL. V FEBRUARY, 1910 NO. 1

THE TROPICAL SUNLIGHT.[1]

By PAUL C. FREER.
(From the Bureau of Science, Manila, P. I.)

INTRODUCTION.

I have chosen my topic for discussion, not only because I knew that an audience, every one of whom has had a more or less extended experience in the Tropics, would be vitally interested in it, but also because in the past decade differences, more especially of insolation, in portions of the globe showing contrasts in climate have been the subject of extended monographs and papers appearing in scientific publications and journals. For the greater part, this literature has especially to do with the objective manifestations of the effects of equable temperatures, possible humidity, and supposedly intense sunlight upon the conditions of life of human beings and their response to their environment. Considered in this aspect, there always enters an element of uncertainty owing to the absence of absolute means of measurement and the variability of other hygienic surroundings. The people of the Tropics, by reason of their mode of life, their food, their backwardness in scientific procedures and their superstitions, are exposed to many infections and causes of disease which modify any conclusions which may be drawn, and these effects, because of their omnipresence, reflect themselves upon the modern European intruders. Experiments conducted upon the influence of this or that type of clothing, on the modifications of covering upon troops in the field and other similar lines of investigation always suffer from the factor of the condition of the subjects themselves. The impossibility of introducing any exact comparisons into these experiments renders the conclusions drawn therefrom arbitrary.

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[1] Address of the president at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 5, 1910.

However, in almost all cases, differences in the environment brought about by contrasts between tropical and temperate climates are referred in the first instance to the sunlight, in the second to humidity, if this factor is taken into consideration at all, and in the third to the equable temperature throughout the year; that is, to the absence of a pronounced winter.

It has seemed to me that the first of these factors, the sunlight, is capable of some exact comparative measurements, although, from the nature of the case, the experimental difficulties in the way are very great. To draw any final conclusion, work with reliable and calibrated instruments must be undertaken in various parts of the globe, through a long series of days, and experiments must be planned so as to eliminate, so far as possible, the personal errors which may creep in. We must take into consideration the average number of hours of sunshine per day, the degree of haziness or cloudiness, the variation with the seasons, the presence or absence of pronounced winds and the proximity to the seashore of the stations as well as their altitude. Needless to say that, while many individual observations exist, no comprehensive plan of work, based upon data taking cognizance of all of these factors, has ever been carried into effect. In order, if possible, to make a beginning, I have brought together the results of the investigations which we have been able, so far, to conduct in this institution, together with such as may be pertinent to the question obtained in other places. The sum total leaves us with only a few facts gained and a few conclusions to be drawn, but it shows to a certain extent what direction it is best to follow in coöperative work and it also reveals to us the complexity of the field.

THE SUNLIGHT.

We all know that the sunlight can be dissolved by proper instruments, such as a diffraction grating or a prism, into an infinite number of waves or pulsations of different length, which produce a continuous visible spectrum extending from deep red to violet; this spectrum being crossed by numerous sharp lines, representing the absorption phenomena of the elements existing in a gaseous state in the sun. On either side an area not visible exists, the infra-red and the ultra-violet. The latter portions of the spectrum can be studied by means of photographs. Measurements are made in millionths of a millimeter, starting from some well-known line which may be produced between two poles of a given metal by a spark caused by a current of high tension. If we compare the spectrum of the sun's light with that of a metal, such as cadmium, we discover that the latter shows lines extending into the ultra-violet field far beyond that of the former, yet it is evident, if we consider the elements known to be present in the sun's mass and chromosphere, by a study of the spectrum of the sunlight, that outside our atmosphere, or at least in the central body of the sun, such ultra-violet rays must be present. It follows that the air surrounding our globe must be able to absorb or otherwise modify a large proportion of the latter. Measurement can show whether, as a rule, there is a greater or less absorption in the Tropics than in temperate climates.

The theory was prevalent some years ago that the spectrum was divided into classes of rays, of which those in the blue, violet and ultra-violet were considered as "actinic," namely, as producing chemical reactions, those in the visible field as causing light, and those in the ultra-red as heat, although even as long ago as 1859, Bunsen and Roscoe [2] indicated that no sharp lines could be drawn between the rays which give rise to the thermic phenomena in the atmosphere and on the earth, and those causing chemical changes. The power of seeing is only a subjective symptom, some persons may have a range of vision for light rays beyond others; all rays may produce chemical changes, yet it is true that some of the latter are brought about much more rapidly by the portion of the spectrum lying toward the violet and beyond, than by the other part toward the infra-red; indeed, in many changes the latter can not act as a catalyzer at all. However, we must not lose sight of the fact that the total energy derived from the sun, in which must be included rays of all lengths, is an essential factor in maintaining chemical changes on the earth, regardless of the fact that recent investigations have made us cognizant of other sources of energy which are supplied by the mass of the globe itself. The quantity in which the former reaches the earth's surface at different places may have much to do with the effect of local environment.

In studying the manifestations of energy in other branches of science, we endeavor to divide such manifestations into two factors, one of intensity or stress, and the other of capacity. So, in electricity we have volts (stress) and coulombs (capacity); in the effects of gravity, distance (stress) and mass (capacity). Light can be treated in the same way. Let us suppose we have an area of 1 square centimeter through which rays of a given wave length are passing from a constant source of light. If we double the opening, we would have twice the light passing through, but if we concentrate the total number of rays entering the opening of 2 square centimeters, by means of an ideal lens, on the one we would obviously have doubled the amount of light in the same time passing through the slit, the area of which had not changed, in other words, we would have increased the intensity of illumination, or the amplitude of the light waves, a process corresponding to an increase of voltage, with diminution of the diameter of the cross section of the wire, in an electric conductor. While it is easy to conceive of measurements of this kind where rays pass through a definite, limited opening, it is not so easy to see how they can be made when the illumination extends over a vast area. Bunsen and Roscoe[3] and Roscoe and Baxendell,[4] in their classical researches on photochemistry, employed an explosive mixture of chlorine and hydrogen to measure the intensity of insolation, and by a variation in the quantity of light, by using different sources and different diameters of openings, came to a series of results which, more nearly than any other, can be used as a basis of calculation. However, it seems to me that the possibilities of autocatalysis in such a mixture,[5] which have since then become understood, would have a great influence in the calculation of the total effect of insolation in climates other than the one in which these investigators worked. Subsequently, they also perfected a method based upon the darkening of a normal strip of sensitized paper in known intervals of time to standard colors, and this means, if the paper were always correct, could be developed in the direction mentioned. Indeed, Roscoe[6] described a self-registering apparatus for use in meteorological stations which would, if universally adopted, already have made available the data sought for. However, it seems to me that all methods which consider "photochemical" light only as a group, without division by the spectrum, are faulty because they do not differentiate the proportion of waves of various lengths contained in the total insolation at different latitudes and under different meteorological conditions. The range of rays which will bring about the union of hydrogen and chlorine, or the darkening of sensitized paper, is very great, whereas it may be only certain very limited portions of the spectral field which produce maximum results.

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[2] *Ann. d. Phys. u. Chem.* (Poggendorf) (1859), **108**, 193.

One method suggests itself. If two spectra of the sun, each showing the same area, that is, composed of waves of the same length, were to be projected upon two extremely slow photographic plates, so slow that, although the plates are approximately the same, slight variations in time would have no appreciable effect upon the total exposure, and if comparisons were to be made as to the time necessary to produce the first visible image of some given line, then the ratios of these times would, for most practical purposes of comparison, give the ratios of intensities. The accuracy would increase by selecting more than one line, successively.

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[3] *Loc. cit., ibid.* (1862) **117**, 529.

[4] *Ann. d. Phys. u. Chem.* (Poggendorf) (1866) **128**, 291.

[5] Chapman, Chadwick and Ramsbottom, *Journ. Chem. Soc. London* (1907) **91**, 943, give a parallel case in the reaction of carbon monoxide and oxygen in the presence of moisture. Hydrochloric acid takes the place of the latter.

[6] *Ibid* (1877) **151**, 268.

However, other chemical reactions could be selected, perhaps with less experimental difficulty, provided all side reactions, such as oxidation or peroxide formation, were eliminated. Such a reaction is the decomposition of oxalic acid in the presence of uranium acetate as a catalyzer, the gas evolved in a given time by given rays being measured, or the residual oxalic acid titrated. This reagent for the measurement of the two factors of the sunlight without, however, as yet using definite lines, has been utilized by Dr. Raymond F. Bacon, of the Bureau of Science, he being able to compare the insolation at Chicago, in June, with that of Manila throughout the year. I will discuss his results in another portion of this paper. The method being fully developed, subsequent experiments, using definite lines of the spectrum will be a simple matter.

His measurements, although extending over a limited period in Chicago, are nevertheless of such a nature that we have an experimental comparison between the effect of insolation in the Tropics and at a northern point. Previous attempts have been made to calculate the effect from the data of Bunsen and Roscoe,[7] taking into consideration the direct and diffused sunlight. The calculations result in the development of numbers showing that "diffused light tends to equalize the numbers for the total quantity of light at different latitudes." So, according to Sebeliene,[8] while "the daily quantity of light due to direct radiation is forty times as great at the equator as it is at the pole, the quantity of diffused daylight is hardly twice as great at the equator as at the pole on the same day." The results of Sebeliene's calculations, based on Bunsen and Roscoe's figures, give a total quantity of light units at 0° of latitude as 82,716, a maximum of 114,835 at 30°, and a minimum of 76,048 at the pole. However, these calculations refer only to the midsummer day, and certainly lack the basis of experiment in various parts of the world. While the northern and southern parts of the globe are much more fortunately situated at midsummer in respect to light, as compared with the Tropics, this would not hold good throughout the year. Bacon, in the Bureau of Science, found the decomposition of oxalic acid in the presence of uranium acetate to proceed approximately five times as fast in Manila in October and November as in Chicago during the months of May and June; and recent days in February have shown a rate as high as twenty. Bunsen and Roscoe[9] also demonstrated that days of light, hazy cloud, through which the sun just shines, are able remarkably to increase the chemical activity of light.

Enough has been said to demonstrate the difficulties to be encountered in securing data fit for comparison; the experimental work so far accomplished, therefore, is as yet only tentative and must be taken for what it is worth.

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[7] *Loc. cit.* (1859), 108, 257, 260.

[8] *Phil. Mag.* (1905) (VI), 9, 354.

[9] *Loc. cit.* (1859), 108, 236.

THE COLORATION OF PHENOL, OF ANILINE, AND OF METHYL ALCOHOL IN THE SUNLIGHT OF MANILA.

All of us who have experience with laboratories in the Tropics presume, in a general way, that chemical reagents are much more subject to deterioration and change in such regions than in temperate climates, although the containers may be securely sealed from the air. Is this so, or is it simply a hasty generalization, brought about by our personal bias, driving us in the direction of thinking the phenomenon must really exist because of preconceived notions of the influence of tropical environment?

Phenol is eminently fitted for study, because some data for comparison, gathered in other climates, exist. Mr. H. D. Gibbs,[10] of the Bureau of Science, has occupied himself with this subject for more than a year, and I will give a brief summary of his results.

The phenomenon of the coloration of phenol in the sunlight is one of oxidation, it does not occur in an atmosphere of an indifferent gas such as hydrogen or nitrogen. The change takes place even with absolutely pure, dry phenol and dry oxygen, so that the presence of moisture is not necessary. The reaction, under ordinary conditions, therefore, is inaugurated independently of the degree of humidity of the atmosphere, although the water (or hydrogen-peroxide) produced by the beginning reaction will undoubtedly have an accelerating effect on its subsequent rate. Crystals of such pure, dry phenol, when sealed in a tube with pure, dry oxygen and placed in the sunlight in Manila at a temperature of approximately 30°, color perceptibly after two hours and the entire mass changes to a deep red liquid after five days.

This rate of coloration probably varies with the seasons. When the sun is directly overhead there is apparently a much more rapid production of color than in December and January; and it is more rapid under quartz than when the sample is exposed under soda glass. This latter difference would seem to point to the fact that the change is inaugurated by and accelerated in a greater degree by the ultra-violet portion of the spectrum, not absorbed by quartz glass, than by the others, although the effect can be brought about by heat alone, but much more slowly.

The absorption spectum of phenol[11] gives a broad absorption hand at $\lambda=272$ $\mu\mu$. There is, therefore, according to Baly and Collie,[12] a condition of unstable equilibrium of one hydrogen atom in each molecule of phenol, at a given temperature in the dark. Therefore there would be a constant ratio between the large proportion of phenol in the enol form and the minute quantity of the keto (quinone) form. The action of light, especially of that of the ultra-violet portion of the spectrum, would therefore be to change the equilibrium by increasing the proportion of the latter present, and hence the rate of oxidation; it being presumed that the enol form, the one ordinarily accepted for phenol, is not attacked by the oxygen. No quinone form seems to be present in the crystals. Anisol is not colored by oxygen or ozone in the presence of sunlight, hence it is to be presumed that no such labile form exists in the latter.

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[10] *This Journal, Sec. A* (1908), 3, 361; *Ibid.* (1909), 4, 133.

[11] Hartley, *Journ. Chem. Soc.* (1902), 81, 929.

[12] *Ibid.* (1905), 87, 1339.

The color change of phenol takes place much less rapidly in temperate climates where measurements have been made. Richardson gives three days in Clifton, England,[13] and in some instances several weeks have not sufficed to produce the color. A tube of phenol and oxygen, in the dark, kept at a temperature of 100° for two weeks, gave only a faint yellow color, and phenol under the same conditions in the diffused light of a laboratory room at Manila at a temperature of approximately 30° was not appreciably colored after two months.

The products of oxidation are quinol, quinone and catechol, all of which confirm the conclusion that the change to the quinone formula is markedly accelerated by the ultra-violet rays which are absorbed by phenol and point in the direction of the supposition that these rays are present in greater proportion in the sunlight of the Tropics, at sea level, than in more northern climates. The conclusion in regard to the labile condition of one-sixth of the hydrogen in phenol would probably also be found true for a large series of similar compounds, and may, possibly in the future be extended so as to explain a great many chemical phenomena prominent in tropical climates.

Aniline is even more fitted than phenol for a study of the effects of insolation, as the changes are brought about with greater rapidity and the oxidation products are present in greater quantity.

When perfectly pure aniline is sealed in a thin glass tube with dry air and exposed to the sunlight in Manila during the months of April, May and August, it darkens and assumes a decided red shade in less than ten minutes. Of course, the temperature, as in the case of phenol, is also an important factor.

The products of the reaction which have been isolated are azobenzene, 2,5-dianilinoquinone, 2,5-dianilinoquinoneanil, and azophenene. The oxidation is therefore in all probability accompanied by one of condensation, and again it seems not unreasonable to refer the rapid accomplishment of this portion of the reaction to the part of the spectrum lying in the violet and beyond.

Pure samples of aniline also became colored upon long standing in the dark. Aniline, like phenol, therefore, has a portion of its hydrogen labile and probably shows a similar equilibrium between the ordinarily accepted formula and the quinoid structure as is presented by phenol. Its absorption spectrum also gives a deep band in the violet.

However, aniline differs from phenol in the fact that in the tropical sunlight it undergoes chemical changes even in the absence of oxygen, that is, when it is placed either *in vacuo* or in the presence of indifferent gases such as hydrogen, nitrogen, or carbon dioxide. At first it is colored yellow and finally it changes to a brilliant red. The work on this subject is not entirely completed. However, it may be stated that no gas is evolved, azophenene is the main substance formed, and ammonia is also present. The sunlight therefore, in this climate, produces a profound decomposition of aniline, oxidation to azophenene and simultaneous reduction to ammonia and probably benzene taking place. No data for comparison with the same reaction as produced by the sunlight of temperate climates are at hand, but it is safe to presume that a change of the kind just mentioned does not take place except with extreme slowness in northern latitudes; at least none of us have ever become aware of it before working in Manila.

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[13] *Journ. Soc. Chem. Ind.* (1893), 12, 415.

Mr. Gibbs has also taken up the study of the oxidation of methyl alcohol in the sunlight and has shown that formaldehyde is readily produced in this climate, although in other, more northern portions of the earth, no reaction at all could be noted under these conditions. Methyl salicylate is also colored in the sunlight of Manila with a fair degree of readiness, the methyl alcohol produced by the hydrolysis of the ester being oxidized to formaldehyde and the latter condensing with the derivatives of salicylic acid to produce a dye.

All of the reactions which have been mentioned are still the subject of investigation, but enough has been brought out to render certain that the tropical sunlight, in fact, produces chemical changes which either take place much more slowly in temperate climates, or indeed do not take place at all.

THE DECOMPOSITION OF OXALIC ACID BY SUNLIGHT IN THE PRESENCE OF URANIUM ACETATE.

In order, if possible, to obtain a quantitative estimate of the effect of the sunlight at this latitude, and to institute comparisons between this effect and that to be observed in the more northern portions of the United States, Dr. Raymond F. Bacon, of the Bureau of Science, has modified the method adopted by Duclaux.[14]

The latter author, subjecting oxalic acid to the action of the sunlight, in the presence of oxygen, in various parts of the globe, encountered the following remarkable facts.

> Two months of uninterrupted observation showed that the solar combustion passes through very different values within twenty-four hours. These changes are sometimes very sudden and exceed, especially those of the thermometer, the barometer, and even those of the average brightness of the day.
>
> So, for example, on a fine day without clouds, there was 34 per cent of the solution of oxalic acid destroyed, while, only five days earlier in the year, on a day with slight cirrus, 35 per cent were burned. A bright day in October showed 12 per cent as against 20 per cent when the sky was cloudy during the entire time of exposure, and even greater contrasts, from 7 to 28 per cent, were observed on days entirely similar to all outward appearances. The maximum decomposition appears to be in the spring.

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[14] *Smithson, Contrib. to Knowledge* (1903), 29, 1034.

> Comparisons made in August between St. Pierre le Port, on the Channel, and Helsingfors (latitude 60° 10′) gave as a maximum 44 per cent of decomposition in France and 77 per cent in Finland, between the hours of 8 and 4. a most remarkable result, tending to show that the chemical effect of the sun's rays, in late summer, is greater at the far northern latitude of Hesingfors than in France. In Algeria, during the same months, the maximum was only 14 per cent. According to Duclaux's experiments, therefore, the chemical effects of the sun's light diminishes in the summer months as we proceed from a northern climate toward the equator.

The above results do not hold good in Manila. Here, following the method of Duclaux, Doctor Bacon has found that, using 10 cubic centimeters of $\frac{N}{10}$ oxalic acid, the decomposition of oxalic acid, between the hours of 8 and 4, is almost always practically complete. Thus, the figures for four days are 68, 96, 85, and 100 per cent, respectively, and even on a day over one-half of which was cloudy (January 19), complete oxidation had taken place by 5 o'clock in the afternoon. While there is no doubt as to the results obtained by Duclaux in the dry climate of Algeria, near a great desert, it certainly is true that those reached in Manila are contradictory to the ones which have been quoted, and that there is here a marked increase in the rate of decomposition.

However, the oxidation of oxalic acid in the sunlight suffers from a great defect. Duclaux noticed that a solution when first exposed decomposed very slowly and that the reaction is subsequently rapidly accelerated. We have shown here that this phenomenon depends on the formation of hydrogen peroxide, and that the increasing rate is due to autocatalysis. While the method, therefore, gives a certain measure of comparison, it is not above criticism.

The decomposition of oxalic acid in the presence of uranium acetate is not dependent upon oxidation, and is not accelerated by autocatalysis, and is therefore much better adapted to comparative study.[15] Doctor Bacon also had the good fortune, while in America on leave, to compare this reaction in Chicago with that in Manila. The time in Chicago was during the months of May and June; the total average extending over ten days gave, for Chicago, approximately 100 cubic centimeters of gas in two hundred minutes, and in Manila, with the same solutions, 100 cubic centimeters in forty minutes. It is also at present noticeable, in this climate, that as the altitude of the sun is increasing, the decomposition is accelerated; thus, January, 1910, gave an average decomposition of 0.081 gram of oxalic acid per hour as compared with 0.090 in the middle of February. The optimum day in Manila has far exceeded the ratio of 5 to 1 observed above, and has more nearly reached 20 to 1.

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[15] Raymond F. Bacon. *This Journal, Sec. A* (1907), 2, 129.

ACTINIC AND NONACTINIC DAYS.

The differences between various days apparently similar in every respect as regards insolation is very remarkable, and what is still more striking, hazy days seem often to bring about greater decomposition of the oxalic acid than those which are perfectly clear; conditions which had previously been noted by other authors referred to in this paper.

A table will make this more evident.

TABLE I.—*Decomposition of oxalic acid in the presence of uranium acetate.*

No.	1910.	Decomposition, grams of oxalic acid.	Day.
1	Jan. 17	0.084	Bright sun.
2	Jan. 18	0.083	Hazy.
3	Jan. 19	0.049	Partly cloudy.
4	Feb. 4	0.080	Partly cloudy, but on the whole fair.
5	Feb. 5	0.050	Bright sunlight.
6	Feb. 7	0.035	Sun intermittent but still partly bright.
7	Feb. 8	0.045	Hazy and cloudy.
8	Feb. 9	0.075	Hazy and cloudy.
9	Feb. 14	1.000	Bright sunlight.
10	Feb. 16	0.085	Partly cloudy.
11	Feb. 17	1.120	Bright sunlight.
12	Feb. 18	0.041	Cloudy.
13	Feb. 21	0.047	Cloudy.
14	Feb. 22	0.073	Bright sunlight.
15	Feb. 23	1.500	Bright sunlight.

It is feasible, therefore, to divide even the days of bright sunshine into those which are "actinic" and others which are "nonactinic." Thus, numbers 9, 11, and 15 are distinctly actinic, whereas number 5 and 14 are nonactinic; undoubtedly the effect of insolation in the Tropics during the former would be much greater than during the latter; indeed, some of the nonactinic days are very nearly like those of temperate climates.

THE EFFECT OF TROPICAL SUNLIGHT ON THE ATMOSPHERE.

Another phenomenon to be observed in Manila in a marked degree, and which, so far as I am aware, has not been recorded in the literature from other climates, is the extensive ionization of the air when exposed to the sunlight. Doctor Bacon, using a modern electroscope, has been able to show that our atmosphere, when exposed to the direct rays of the sun, rapidly discharges the instrument, the loss of potential being 46 volts per hour, whereas, in the diffused light of a room it is only 15, and during the night 6, for the same volume of air. This is certainly a remarkable result, which deserves further study. The only comparative data on hand are a few by Elster and Geitel[16] giving us an indication of what the fall of voltage would be in northern climates. They found, in Vienna on a foggy day, a voltage of 2.77, in clear weather, 8.58, but on a day when the sky was half overcast, 13.67. These authors ascribe the phenomenon to radio-activity, but our results in Manila, where radio-active phenomena are not especially prominent, would lead to the conclusion that the air is ionized by sunlight. The presence of this ionization in so great a degree in our atmosphere would indicate a condition of the solar spectrum which might well account for many of the so-called excessive effects which have been observed.

THE EFFECT OF SUNLIGHT ON MICROÖRGANISMS.

A great mass of literature exists on this subject, but the later publications of Hertel[17] have brought the study down to such a clear basis that it seems scarcely necessary to enter into the work of previous authors with any detail. Suffice it to say, it is a fairly well established fact that bacteria and even their spores are destroyed by sufficient exposure to the sunlight. Of course, the time necessary for this effect varies greatly with the latitude and the degree of insolation, and naturally the errors of observation are very large.

The general method of procedure has been to expose plate cultures or tubes to the direct action of the sunlight during fixed hours, placing controls in the incubator, and covering either portions of the plates or tubes, or their contents where needed, by tin foil. Of course, in the majority of published researches, care was taken to exclude heat action by proper precautions. Different colors were produced by colored plates or solutions, in some instances spectroscopically examined. But few of the authors have used quartz prisms and lenses to give a spectrum. It is well known that glass absorbs the ultra-violet of the spectrum.

Hertel undertook his experimental work not by employing the entire sunlight, or by blending with colored glasses, but by the spectrum of the sun from the ultra-violet region, using an apparatus the parts of which were constructed of quartz, testing the action of the light within different, but sharply defined regions of determined wave length. The first source of light employed was the bright line from magnesium at $\lambda = 280\ \mu\mu$.

Bacteria and vibrios (*B. coli*, *B. prodigiosus*, the vibrio of cholera, *B. typhosus* and others) in the first moments of illumination by this portion of the spectrum, increased in motility, that is, gave evidence of stimulation, but after a few seconds there was a retardation and finally complete rest. The bacteria of decay also were markedly affected, with final death. Especial experiments demonstrated that the light had no effect on the culture media, so that the sterilization resulted because of the action of the radiant energy on the organisms alone.

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[16] *Ann. d. Phys.* (IV), 2, 425. The authors used an instrument of identical form with our own.

[17] *Ztschr. f. allg. Physiol.* (1904), 4; (1905), 5; (1906), 6; *Rev. in Biol. Centralbl.* (1907), 27, 510.

Paramecia, when exposed, showed an instantaneous state of unrest, with a tendency to escape from the illuminated field, longer illumination finally brought about their complete decomposition. Nematodes were more resistant, death following only after two or three minutes. Larvæ of amphibia showed a decided wandering of pigment toward the spot in contact with the light. All of the organisms investigated had a marked reaction toward light of 280 $\mu\mu$, first in increased motility or contraction of contractile tissues, followed by lassitude, slowness of motion and final death. Toxins and ferments were also tested, so, for example, the toxin of diphtheria was rendered entirely inert after five minutes; trypsin, diastase, and the ferment of rennet were also profoundly affected, but not in as great a degree as the toxins.

The experiments next were extended to lights of various wave lengths, the total energy of each region of the spectrum being measured thermo-electrically, it developing that *"the action of one and the same spectral line is directly proportional to its total intensity, as measured thermo-electrically."*

The physiological action of the rays diminishes with increasing wave length, a difference of 50 $\mu\mu$ showing a marked effect. Light of 280 $\mu\mu$ kills organisms almost at once, whereas that of 440 $\mu\mu$, of equal intensity, does so only after a number of hours of action.

Perhaps the most important result of Hertel's work, for our present purposes, is his proof that not only the total energy and the wave length of the incident light are of importance, but also the relative proportion of the rays absorbed by the organisms, for he developed the fact that the absorption of radiant energy by the tissues of the organisms investigated is diminished the longer the wave length of the light which is employed.

The action of a specific kind of light on organisms is therefore not only dependent on its total intensity, but is also in the greatest degree related to the power of absorption for this light possessed by the tissues. By means of erythrosin Hertel was able so to stain the cells of living organisms that their power of absorption for waves of greater length than 280 $\mu\mu$ was markedly increased. The introduction of this experimental modification enabled Hertel to demonstrate that even the visible light rays could bring about destruction of tissue in the same time as the ultra-violet.

The physiological action of light rays is therefore not dependent upon any specific region of the sun's spectrum, the wave length is only of importance in such degree as the total energy, and the power of absorption is determined thereby. A plant, for instance, for the existence of which light is absolutely necessary, takes on a color which is complementary to the incident rays, for example, *Oscillaria sancta* colors red in green light and green in red. Light also has an unfavorable effect on the phenomenon of cell division, but this only takes place with higher intensities. Different pigment cells have a different absorptive power for incident light, according to its wave length, but the ultra-violet rays are equally absorbed by all. Therefore, the latter differ markedly from visible light, in which the absorption maxima, according to the color, lie at diverse and far-removed parts of the spectrum.

The character of the pigment, therefore, is of fundamental importance in determining the effect of insolation for all save the ultra-violet rays; but the experiments of Baly on chemical substances, in distinction to those of Hertel on the pigments of natural tissue, have shown that the absorption of the former for ultra violet light differs markedly according to the nature of the chemical individual employed.

While Hertel's investigations have no direct bearing, at present, on the subject of tropical sunlight, because concrete and connected experiments in the Tropics are lacking, still the coloration of phenol and aniline, the oxidation of methyl alcohol, the rapid decomposition of oxalic acid in the presence of uranium acetate, and the intense ionization of the air in Manila, are possibly referable to a larger proportion of ultra-violet light in the sun's spectrum at this latitude; and therefore, if this be so, it will also be true that living tissues will be affected abnormally, or, in other words, we should expect the effects of tropical sunlight upon micro-organisms and those of a higher order, and the consequent endeavor by pigmentation or other means of these organisms to protect themselves, to be similar to those observed by Hertel for the ultra-violet in his spectroscopic investigations. Of course, we must not lose sight of the fact that the tropical sunlight probably displays a greater intensity of all rays, and that this effect would be cumulative.

Ewart[18] calls attention to the fact that plants in the sunlight of the Tropics seek to protect themselves by the production of a red color (erythrophyll) the absorption spectrum of which has a band in the violet. In a journey to Java he observed that the red color of the leaves was more common and marked in the low, tropical valleys than higher up on the mountains. In the cloud-covered belt it was entirely absent, but above the latter it again appeared.

However, it has not been proved that the tropical sunlight really does contain a greater proportion of ultra-violet light than that of northern climates. So far, we can only come to the conclusion that it has a greater intensity, as the experimental work which I have given has shown, and that a certain proportion of rays lying in the ultra-violet is present. Greater intensity, although with but a small area in the latter portion of the spectrum, would bring about results similar to those which would be observed if the light extended to 280 $\mu\mu$ beyond.

THE SPECTRUM OF THE SUN IN MANILA DURING FEBRUARY, 1910.

We have endeavored to solve this problem in Manila by the construction of an instrument from such means as are at hand. Funds have heretofore been lacking to have made by the best mechanics of America or Europe a spectro-photographic apparatus entirely adapted to the needs of the investigation.

Our spectroscope consists of a Rowland grating, a heliostat, both very kindly loaned to us by the Philippine Weather Bureau,[19] and a quartz lens and slit taken

[18] *Journ. Linn. Soc.* (*Bot.*) (1895), **31**, 364; *Ann. Bot.* (1897), **11**, 440.

[19] I wish at this place to express my sincere thanks to the Reverend Father José Algué, Director of the Weather Bureau, at Manila, for his loan of apparatus and his most kindly coöperation in all that we have asked of him.

from a Zeiss ultra-violet photomicrographic apparatus. The three are mounted in a line upon a prism base, and the image of the spectrum is projected upon a camera placed at one side, and in the plane of the slit. The necessary motions of camera, lens and grating are provided, but, unfortunately, we can not work with curved plates, so that only a small portion of the spectrum is in focus at one time. The whole apparatus is inclosed in a light-tight box and secondary spectra are excluded by an appropriate shield within the box. (See fig. 1.) The use of the heliostat can be avoided by pointing the apparatus directly at the sun.

The spectra obtained at noon are shown by Plate I. They do not probably extend beyond $\lambda=291\ \mu\ \mu$, and therefore not much farther than has been observed by others. Measurements undertaken by Miethe and Lehmann[20] in Assuan, Berlin, Zermatt, Gornergrat, and Monte Rosa give practically identical numbers, namely 291.55 $\mu\mu$ to 291.21 $\mu\mu$ during the latter part of August and the first part of September; these authors finding, in contradistinction to the observations of Cornu,[21] that altitude above the sea level makes no great difference. As one of these places is at 24° 30′ north latitude, where the others are in northern climates, it is evident that as the extent of the ultra-violet field does not change materially, the intensity factor in the solar spectrum must vary to a great extent in different places. However, it is possible that a considerable range of ultra-violet is absent at present (March 1) from our sunlight. Probably this area will increase as the angle of the sun diminishes and as the season advances; and it may reach a maximum in April, although these recent results would seem to indicate that even here we will not get below 288 $\mu\mu$.

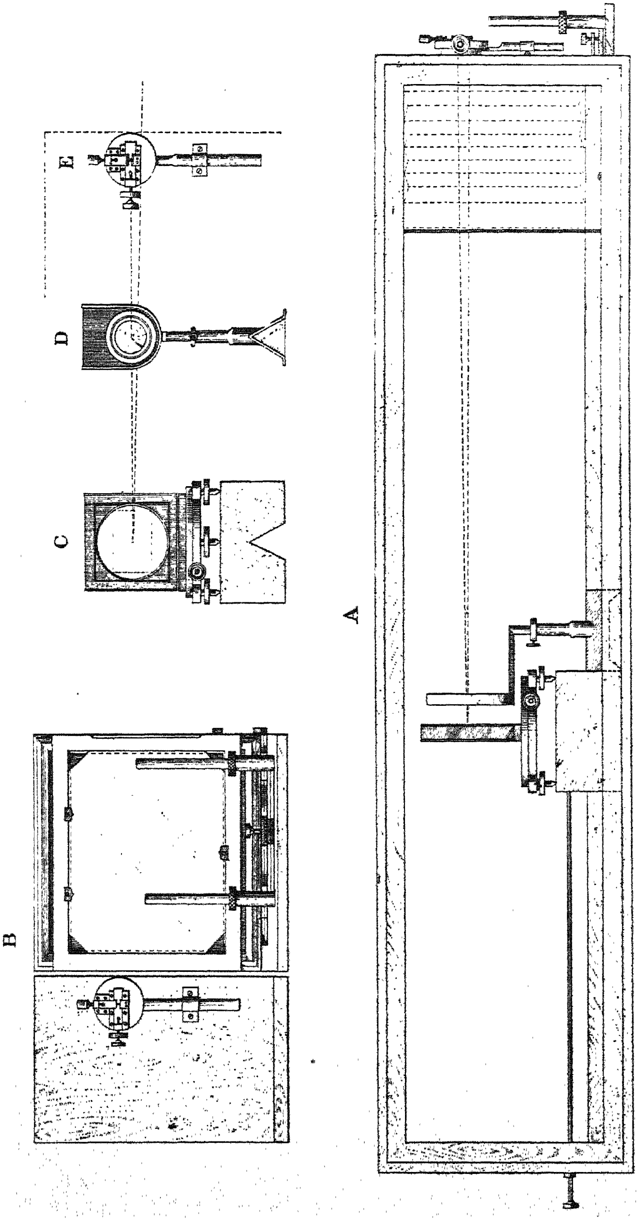
Enough has already been demonstrated to prove that the emphasis placed upon the ultra-violet spectrum in the preceding part of this paper is justified.

GENERAL CONSIDERATIONS.

If we consider the equator as being in one plane and the poles in another, normal to the incident rays of the sun, it is obvious that the relative distance between these two points is practically infinitely small as compared with the distance of the sun from the earth. If we regard this phase alone, obviously the insolation at the equator and the poles would approximately be equal. However, these two positions are on different points of a sphere, which is surrounded by the atmosphere, so that not only is the angle of incidence of light rays different in different regions, but also, as they pass from the ether into the atmosphere at different angles, they suffer refraction in differing degree. The shorter wave lengths, in this respect, are influenced to a greater extent than the longer, and, under proper conditions, are even finally totally absorbed or reflected, so that none would reach the earth. This condition would

[20] *Sitzungsber. d. k. Pr. Akad. d. Wissensch.* (1909), **8**, 268.

[21] *Compt. rend. Acad. Sci.* (1879), **88**, 1107; *ibid* **89**, 808.



× ¼

FIG. 1.

come about the more readily, the greater the number of layers of the atmosphere of different densities which exist at any given place. So, in northern climates, where irregular and high winds may prevail, strata might be produced in great numbers by meteorologic conditions, and as each layer or stratum has a different density from the one above or below it, it would take its part in the total amount of refraction. Where the distribution is fairly equable as it is in the region of the trade winds, we would expect a greater proportion of the waves of short length to pass the atmosphere to the earth; at about 30° of latitude accurate observations will probably discover locations in which the sun has great actinic power. At the equator, where the great mass of heated air rises to flow toward the poles, while the air from the north and south passes in, we may have what might be termed an atmospheric lens effect, serving to concentrate the rays of the sun, as they pass from the rarer to the denser medium, and thus giving more intense insolation. In this discussion the modifying factors of diffused light, and of that reflected from the earth, are not taken into consideration, obviously these will vary greatly, and will be much influenced by local conditions.

Although we may conclude,. from the experimental data given in the preceding portions of this paper, that insolation in our regions is really of greater intensity than it is in northern climates, we must also note that the measurements of value in determining this question are undertaken on days of bright sunlight or of slight haze. It has already been shown that the latter are often more "actinic" than the former, perhaps because of reflection of the sun's rays which reach the earth, thus increasing the total quantity of light over that which would be present on a clear day. This, however, does not account for the differences observed between two equally clear days at the same time of the year, one of which may be "actinic," the other "nonactinic."

What causes this difference? Is it brought about by air currents of differing density, causing refraction or even total reflection of a portion of the light? Is it due to some disturbance in the chromo- or photosphere of the sun itself? Or, again, has the phenomenon of ionization of the air, by absorbing the radiant energy for this purpose, a connection with these conditions? I confess I am neither physicist, astronomer nor meteorologist, and must leave the answer to others.. It suffices here to state that this is a fact which must be reckoned with in discussing the total annual insolation of our regions.

Again, when we consider many places in the Tropics, which are regarded, as a whole, as having a climate unsuited for continued residence of European races, we must remember the large proportion of the year in which the sky is overcast. Cloudy days, in distinction from those in which the sun is but partly obscured by haze, naturally show the effects of insolation to a much less degree than days of sunlight, the intensity of the light diminishing with the density of the clouds. The Philippine Weather Bureau has stated to me that, so far as they are aware, twenty-four hours never pass on the Island of Luzon entirely free from cloud, and if we calculate the average number of hours of sunshine in Manila as compared with those of many other places in northern climates, such as Denver or Santa Fe, situated in the Middle West of the United States, we find the figures very must less for this district, namely, for Manila, 51 per cent of the theoretical sunshine as against 69 per cent for Denver and 76 per cent for Santa Fe. Even Chicago and New York present figures higher than Manila, namely, 57 per cent for Chicago and 56 per cent for New York. While, during the clear days, the sunlight may be more intense here, nevertheless many northern climates have, on the average, more hours of insolation, entirely regardless of the lengthening of the days during the summer months as we leave the equator. If we take an entire year we may not have a greater amount of radiant energy here than in many places of the Temperate Zone, and perhaps even less.

To what, then, are the supposed untoward effects of the tropical climate due? Is it perhaps that at certain times of the year we may have a greater intensity of light, although the average may not be any more? If this were true, would not the total result be even more apparent in such regions as New Mexico, or in deserts, in which certainly the sum total of insolation would be larger in quantity than in Manila? Undoubtedly, periods of great light intensity would, during certain times, have their effect in the more rapid destruction of lower organisms, and on plant life, on which only a brief period of excessive insolation would be either destructive or highly detrimental, but is this true of a highly organized being such as man, who, for a large part of the year, is protected, to a greater or less extent, by meteorologic conditions? The results of intense insolation do not seem to be so very apparent in this region; certainly cases of sunstroke are rare.

Much has been done in the way of experiment with clothing and head coverings of various colors, so as to avoid these very same effects, but in introducing any such modification the experimental work of Baly and his co-workers[22] in regard to the absorption spectra for ultra-violet of the various dyes must be taken into account. It does not matter so much what the color of the dye is, so long as it presents a considerable absorption band in the proper region of the spectrum.

It seems to me that in any discussion of the effects of the Tropics, not only the sunlight, but also the general average humidity, the proportion of cloudy and rainy days, and above all, the continued equable temperature without sharp contrasts of heat and cold, must be taken into consideration. Then, too, we must remember that the hygienic surroundings are different here than in our home countries, and in the majority of districts lying in these regions the native population has not, as yet, advanced sufficiently in education to eliminate many of the factors which in themselves may produce a marked effect. Perhaps, when modern methods have been more generally extended, the world may to a large extent alter its opinion in regard to this portion of the globe. Europeans, coming to the Tropics, change their mode of life, and do many imprudent things which bring their after-effects.

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[22] *Journ. Chem. Soc. London* (1904), **85**, 1029; (1905), **87**, 1332; (1906), **89**, 502, 966, 982; (1907), **92**, 1572.

The subject which I have undertaken to discuss is so complex, the experimental work is as yet so little advanced, that I have been able to give only an outline of what may be done, and to suggest lines of investigation for the future. Many of the papers or monographs which have a more or less direct bearing on it I have not been able to quote at all for lack of space. The physicist, chemist, meteorologist and experimental biologist should all combine to bring a clearer understanding into the field; the plant physiologist and ecologist certainly have topics for study for many years to come. If my paper may seem to be inconclusive and simply to bring together a number of nonrelated results, it is because the subject can not, at present, be treated in any other way.

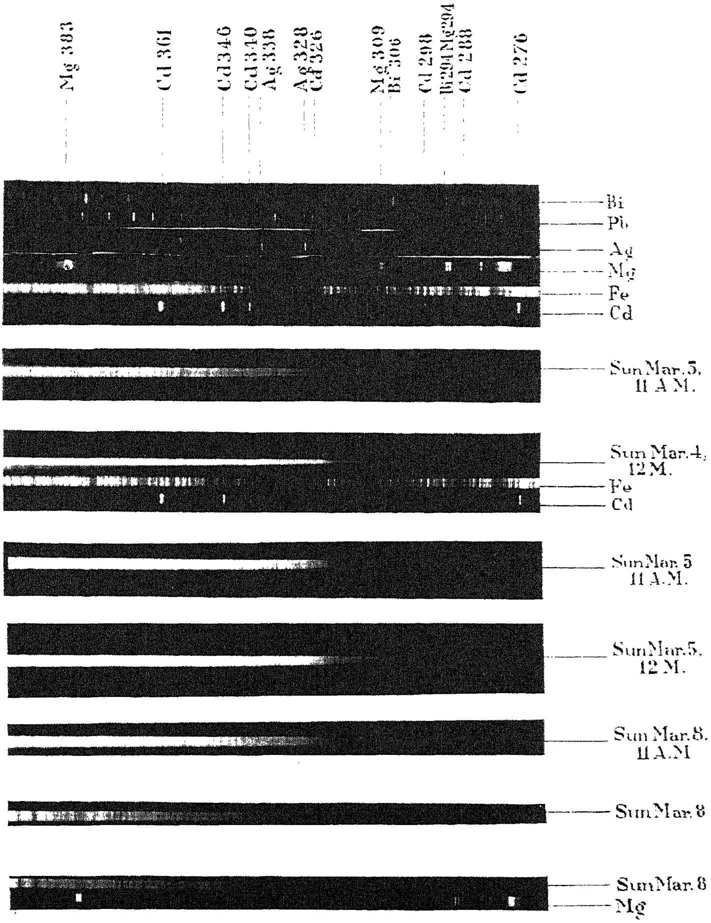
Work on the sunlight will be continued in the Bureau of Science as opportunity affords, and we hope, in the not too distant future, to bring greater clarity into the field. The biological laboratory, with the means now at hand, will also study the effects of tropical light on microörganisms.

ILLUSTRATIONS.

PLATE I. Spectra of various metals and of the sunlight taken with the grating and quartz lens. The lines in the ultra-violet are obscured by reproduction. The print is given to show, approximately, what the instrument will do, and a more complete series will be published in another communication, when better results are obtained.

TEXT FIGURE.

FIG. 1. A. Lateral view of spectroscope; B. End view of slit and camera; C. Grating; D. Quartz lens; E. Slit.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Cd 361
Cd 346
Cd 340
Ag 338
Ag 328
Cd 326
Mg 309
Bi 306
Cd 298
Bi 294 Mg 294
Cd 288
Cd 276
Bi
Pb
Ag
Mg
Fe
Cd
Sun Mar. 5, 11 A.M.
Sun Mar. 4, 12 M.
Fe
Cd
Sun Mar. 5 11 A.M.
Sun Mar. 5, 12 M.
Sun Mar. 8, 11 A.M
Sun Mar. 8
Sun Mar. 8
Mg

PLATE I.

THE TREATMENT OF TRYPANOSOMIASIS WITH ESPECIAL REFERENCE TO SURRA.[1]

By Richard P. Strong and Oscar Teague.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

One of the most important problems that confronts the scientific medical world to-day is the treatment of trypanosomiasis. Sleeping sickness is claiming its thousands of victims each year in Africa. New districts are becoming infected and the disease is on the increase in certain others in spite of the precautions that are being taken. From an economic point of view the loss of horses, cattle and camels from surra and other forms of trypanosomiasis is very large. India, Egypt, Java and the Philippines have suffered severely in this respect. The losses during the epidemic which began in Manila in 1901 amounted to several millions of dollars. Almost all of the large islands of the Philippines have been shown to be infected from time to time with surra, and the loss in horses and cattle has been constant and of no small magnitude. From a theoretical point of view, studies in the treatment of trypanosomiasis have led to the development of a new field in therapeutics, viz, that of "chemotherapy." Since the trypanosomata are motile and live for several hours in defibrinated blood, it is possible to study the action of various chemical substances upon them; such of these substances as prove to be effective against the parasites *in vitro* may then be tested by injection into infected laboratory animals. By these methods it can readily be determined whether or not changes of a given nature in the constitution of an organic compound improve its efficacy against the trypanosomata.

In the following discussion we shall not consider the development of the therapy of trypanosomiasis in chronological order, nor attempt to consider the entire literature upon this subject, but, for the sake of clearness, we shall arrange the more important methods of treatment in the following order and discuss each separately:

I. Serum therapy and vaccination.
II. Treatment with aniline and other dyes.
III. Treatment with compounds of arsenic.
IV. Treatment with compounds of antimony.
V. Treatment with a combination of two or more drugs.

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[1] **Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, at Manila, March 7, 1910.**

I. SERUM THERAPY AND VACCINATION.

Antibodies against trypanosomata have been demonstrated in the sera of animals suffering from a chronic form of the disease and it has even been shown that such sera when injected simultaneously with the trypanosomata of nagana into rats will sometimes protect the latter from infection. However, all attempts to obtain a therapeutic serum against the trypanosoma infections have thus far failed. Laveran and Mesnil (1902) tested the effect of injecting human serum into nagana-infected rats and mice on the supposition that man is not susceptible to nagana. It is claimed that marked improvement followed the injection of human serum. However, the disease in these animals was not cured.

The vaccine treatment, that is, the injection of blood containing killed trypanosomata, seems likewise to have no influence on the course of the disease.

Martini suggested that the inoculation of cattle and horses in infected districts with an avirulent strain of the trypanosoma in question might protect them against later infection with a more virulent form of the disease. In our opinion this would be a very dangerous experiment; for it seems possible that the avirulent trypanosomata might regain their virulence in the course of time and that the "parasite carriers" for which we were responsible might become a fearful menace to all the stock of the district. In this connection it is interesting to note that a number of observers have shown that animals which have recovered from trypanosomiasis by treatment are not immune on reinoculation. Manteufel also found that a previous combined treatment with virulent trypanosomata and a highly immune specific serum does not as a rule result in the production of an efficient immunity.

TREATMENT BY DRUGS.

In observing the results of any form of treatment, usually the more acute the course of the disease, the more readily can conclusions be formed in regard to the efficacy of any particular drug. This fact should be borne in mind in the selection of the experimental animals for testing the various remedies. The extremely chronic character of sleeping sickness in man explains why such a long time has elapsed before anything like a unanimity of opinion with regard to the efficacy or inefficacy of certain drugs has been achieved.

Since small animals very generally tolerate larger doses of medicine in proportion to their body weights than do larger ones, theoretically it should be easier to destroy parasites in the blood of the former than of the latter. It will be seen later in the discussion that this actually has been found to be the case. It therefore follows, and should be borne in mind in the following discussion of the literature, that results obtained on the smaller animals with a given drug can not also be assumed to hold good for larger ones.

II. TREATMENT WITH ANILINE AND OTHER DYES.

The treatment of trypanosomiasis with the aniline colors was introduced by Ehrlich, who first employed coloring matters belonging to the benzopurpurin group for this purpose. A substance (trypan red) was discovered which was found to possess marked trypanocidal properties. Since this discovery considerable attention has been given by numerous observers to the study of the value of other coal-tar dyes belonging to the benzidine (diazo) group, to the triphenyl methane, and to the afridol colors.

However, very extensive experiments have shown that while the subcutaneous injections of trypan red, trypan blue, brilliant green, malachite green, parafuchsin and a few other dyes, into small animals, such as mice and rats, can sometimes permanently free them from trypanosomata, larger animals can not be cured by these drugs. Koch treated a number of patients suffering from sleeping sickness in Africa with trypan red but obtained such unsatisfactory results that he soon discontinued the use of the drug. The administration of the dyestuffs by mouth to experimentally infected animals has given even less satisfactory results than the subcutaneous injections. It is true that Ehrlich was successful in preventing subsequent infection in mice after feeding them parafuchsin and that this work was confirmed by Browning. However, recently Breinl and Nierenstein were unable to obtain any favorable results by such a method in large animals. Two horses were fed on parafuchsin; one received 15 grams daily by mouth for thirty days and died after having shown toxic symptoms from the parafuchsin; the second horse received 15 grams by mouth for forty-eight days. On inoculation it became infected in the same manner as an untreated animal. In our opinion the aniline dyes thus far experimented with are of practically no value in the treatment of sleeping sickness in man, or of trypanosomiasis in the larger domestic animals. This field of treatment seems at the present time practically to be abandoned.

III. TREATMENT WITH COMPOUNDS OF ARSENIC.

It appears that Livingston and Braid, as long ago as 1858, first suggested the use of arsenic for the treatment of horses infected with the bite of the tsetse fly.

Lingard, in 1893, and Bruce, in 1894, also employed arsenic as a curative and prophylactic agent for surra and nagana respectively.

Laveran and Mesnil, in 1902, performed extensive experiments with several arsenical compounds, obtaining the best results with sodium arsenate. With this drug they were able to cause the parasite to disappear from the blood. While the lives of the animals were considerably prolonged, a permanent cure was not effected. Similar results were obtained in the treatment, by arsenic, of horses afflicted with surra in the Philippines by Curry, Musgrave and one of us in 1902 and 1903. Moore, Chichester, Thomas, and Breinl also performed extensive experiments with arsenic and sodium arsenate.

All of this work demonstrated that while the course of trypanosomiasis could be modified and the lives of many of the animals prolonged, with the largest animals, at least, a cure did not result and the disease eventually relapsed. Very severe toxic symptoms and necrosis were frequently produced by the drug. Investigators therefore naturally sought for a less toxic preparation of arsenic and for one which was less likely to cause necrosis.

F. Blumenthal had shown that atoxyl when given to rabbits was forty-five times less toxic than Fowler's solution. Several other observers confirmed these results as to the diminished toxicity of this preparation when compared with arsenious acid. Thomas and Breinl first advanced superior claims for atoxyl as a curative agent in cases of trypanosomiasis after a most searching test on animals. They concluded that it was the only remedy at that time known which gave any promise of a cure.

Almost immediately, numerous investigators undertook the study of the value of this drug and the first reports regarding its efficacy in trypanosomiasis were usually very favorable.

R. Koch treated 986 cases of sleeping sickness; out of 356 cases *positive results* were obtained in 347. The cases were divided into early and advanced. Only the former were affected favorably by the drug.

Favorable results were also obtained by Manson in 5 cases of this disease. Kopke did not secure good results. Out of 29 treated cases of sleeping sickness, 22 died. Only 2 were in good health at the time the report was made.

Ehrlich then showed that many of the relapses after treatment with atoxyl were due to the fact that the parasites had become more resistant to the drug named; they had grown to be "arsenic or atoxyl fast." Ehrlich found after the use of parafuchsin, trypan red and trypan blue that resistant strains were also developed. Moore's detailed and careful studies in the employment of atoxyl soon demonstrated that the efficacy of this drug in the treatment of trypanosomiasis was not nearly so great as might have been supposed from the results of the experiments reported earlier.

In 1909 Moore, Nierenstein and Todd, after extensive experiments with atoxyl on dogs, guinea pigs, mice and donkeys, found this drug entirely unsatisfactory and incapable of saving the animal when employed alone. Brienl also concluded that prolonged experience in the treatment of sleeping sickness in man and, to a certain extent in the experimental animals, has proved beyond doubt that atoxyl by itself effects a really permanent cure in comparatively few and only in exceptional cases of sickness in man, even after it has been administered over a prolonged period, and that nearly all the experiments with horses and cattle infected with *Trypanosoma gambiense* lead necessarily to the conclusion that atoxyl alone is insufficient for a successful issue of the treatment and that it only prolongs life to a certain extent, the animals nearly always eventually succumbing to the disease.

Hodges also concluded that the treatment of trypanosomiasis, or of sleeping sickness, with atoxyl is far from satisfactory and states that its use alone has practically been discontinued in Uganda.

More recent experiments in the treatment of trypanosomiasis have been performed with certain derivatives of atoxyl; one of the most important of these is acetylated atoxyl.

Acetylated atoxyl (arsacetin) was first prepared by Ehrlich and Bertheim, who showed that it was much less toxic than atoxyl for several species of animals and that it could be sterilized without decomposition. Browning believed that animals could withstand ten times the amount of arsacetin as of atoxyl. He also believed that the drug was much more effective than atoxyl in the treatment of infected mice. The experiments by Breinl, however, seem to show that arsacetin is less toxic for animals very susceptible to atoxyl, such as dogs, and that proportionately it is not less toxic for horses and guinea pigs. Uhlenhuth and Woithe confirmed the fact that arsacetin was less toxic for rats than atoxyl. Browning and Wendelstadt, who employed the drug in the treatment of rats, noticed marked tremor a long time after the injection of the drug, in the animals which recovered. Wendelstadt concluded that while rats could be cured with arsacetin, in the large doses required to produce a good result, unfavorable symptoms usually appeared. Moore, Nierenstein and Todd found arsacetin superior to atoxyl. However, when used alone, the animals were not cured by this drug.

The only difference from a chemical standpoint between arsacetin and atoxyl consists in the partial acetylation of the amino group. Kopke has reported it to be very probable that in the treatment of human trypanosomiasis one can obtain with arsacetin the same therapeutic result as with atoxyl, perhaps with less risk of poisoning. Eckard has employed the drug in 134 cases of sleeping sickness. Eighty-six of these were improved, but the cases had not been observed for a sufficient length of time for the author to determine definitely the efficacy of the drug. He considered the drug to be as valuable in the treatment of sleeping sickness as atoxyl.

Apparently, no reports of the use of this drug in the treatment of the larger domestic animals have been published. The consensus of opinion seems to be that it possesses about the same, or a little better therapeutic value than atoxyl.

Experiments with other derivatives of atoxyl, such as salicyl atoxyl, formyl atoxyl, sodium *p*-hydroxyphenyl arsenate, disodium azobenzene 4-arsenate, disodium 4-oxyazobenzene 4-arsenate, tetrasodium phenazine 4-arsenate, sodium di-*p*-acetyl aminophenylarsenate (Breinl and Nierenstein) and with substances closely allied, but having instead of an aniline a toluidin nucleus, for example, orsudan and its derivatives, have also been undertaken, but with no more favorable results.

This concludes the list of compounds of arsenic which have already been extensively employed. The use of arsenophenylglycin, a new preparation, will be considered when our experiments are discussed.

IV. TREATMENT WITH COMPOUNDS OF ANTIMONY.

Plimmer and Thomson suggested the use of antimony, an element chemically closely allied to arsenic, in the treatment of experimental trypanosomiasis in 1907.

They employed the sodium potassium and lithium salts of antimonyl tartrate, of which the sodium antimonyl tartrate proved to be the most efficacious. It quickly caused the disappearance of the parasites from the blood after injection.

Of 39 rats injected and treated with the drug, the majority were living fifty-two days later. This interval is obviously too short to enable a judgment in regard to the final result of the experiments to be made. In more recent work, performed during the past year, these authors state that antimony is as valuable as arsenic in the treatment of trypanosomiasis.

Mesnil and Brimont experimented with potassium antimonyl tartrate in rats and found that the drug caused the disappearance of the parasites from the circulation in about two hours after the injection, but that in many cases they reappeared in the blood. The animals infected with some, but not all, of the species of trypanosomata were cured by this drug.

Boyce and Breinl, however, did not find sodium antimonyl tartrate to give good results either in infected rats or horses. One horse and one monkey were treated with this drug, both eventually succumbed to the disease.

Mesnil and Brimont found in further experiments on mice, that when the animals were treated with tartar emetic, relapses usually occurred, although in the case of the trypanosomata of surra and dourine the parasites disappeared for a time after a single injection of the antimony compound.

Laveran also found tartar emetic unsatisfactory, and sulphide of antimony less active than sulphide of arsenic (orpiment).

Uhlenhuth and Woithe treated 27 rats with sodium antimonyl tartrate. Their results were very discouraging. Repeated injections did not even cause temporary disappearance of the parasites.

Manson has reported the unsatisfactory treatment of one case of sleeping sickness with this drug.

Broden and Rodhain have used soluble as well as insoluble compounds of antimony in cases of sleeping sickness. The hypodermic injections were followed by great irritation and pain so that the drug was given intravenously. Seven hundredths of a gram sometimes caused the disappearance of the parasites from the blood, but they frequently reappeared after a short time. After repeated injections the patients usually lost appetite and complained of malaise. They regard the antimony compounds as about of equal value with atoxyl.

Hodges states that the treatment both with antimony cream and with tartar emetic, singly, has been unsuccessful; that these drugs do not seem to be effective for any length of time and that the treatment of patients with antimony compounds had been discontinued in Uganda at the time the report was made.

Breinl and Nierenstein attempted to prepare an organic antimony compound analogous to atoxyl. After many trials they succeeded in making para, meta and ortho aminophenyl stibinic acids. The ortho compound was impracticable and the meta was unsatisfactory. Extensive experiments with the para compound showed it to be a fairly powerful trypanocide, although not so rapid in its action as sodium antimonyl tartrate. It was less likely to cause abscesses on injection. The authors advise a careful, systematic examination of the urine in the cases treated because of the danger of the production of kidney lesions.

Kopke has treated a few cases of sleeping sickness resistant to atoxyl, with this drug. The injections seemed to cause the disappearance of the parasites, although the author states the inoculations were far too painful for general use.

Laveran has recently suggested the use of an aniline compound of antimony. In potassium antimonyl tartrate potassium was replaced by the aniline radical. Several experiments on guinea pigs seemed to show that the drug was superior to the potassium salt of antimony. A few injections had been made in natives of Senegal, but no final results have been reported.

In the further treatment of sleeping sickness, neither Martin and Rigenbach nor Broden and Rodhain have found tartar emetic administered alone of any great value; the action of the drug after injection is marked, but, as a rule, is only temporary.

V. TREATMENT WITH A COMBINATION OF DRUGS.

A number of investigators who have failed to secure good results in the treatment of trypanosomiasis by single drugs have sought by a combination of two or more to obtain better ones. Some encouragement was given to this idea from the fact that in treating animals infected with trypanosomata, which, for example, had been injected with certain of the dyes or with arsenic compounds and in which dye fast or arsenic fast strains of trypanosomata had developed, injections of antimony seemed more successful owing to the fact that the parasites were not antimony fast. Also, certain drugs which by themselves were inactive against trypanosomata, for example, compounds of mercury or picric acid, when used in combination were supposed to be effective. A large number of experiments have been performed with these various combinations of drugs, but usually with little more definite success than with the remedies employed singly. The following may be mentioned among the combinations of drugs which have been largely employed: (1) Atoxyl and various dyes; (2) atoxyl and bichloride of mercury; (3) atoxyl and tartar emetic; (4) atoxyl and orpiment.

TREATMENT WITH ATOXYL AND ARSENIC SULPHIDE (ORPIMENT.)

Laveran and Thiroux found that a combination of trisulphide of arsenic or precipitated orpiment with atoxyl gave encouraging results in the treatment of guinea pigs infected with trypanosomiasis.

Thiroux and Teppaz treated four horses in this manner, apparently successfully, as all were cured and under observation for six months. The authors state that the animals were infected with a species of trypanosoma other than the one causing surra. Two of the horses were treated with the sulphide alone, neither of these being infected with the surra parasite. Both recovered.

Holmes from India has also reported favorable results with the combined atoxyl and orpiment treatment. Seven guinea pigs and two rabbits infected with trypanosomata received atoxyl and orpiment. In no instance did the trypanosomata reappear in the blood after the first injection of atoxyl. However, four of the guinea pigs died during the period of observation—three months. In the three which lived, four, six and seven doses of the drug, respectively, were given. Seven ponies were also treated with atoxyl and orpiment, given alternately with an interval of one day between each dose. In four, the author reports the treatment to have been successful. Two of the animals of this series and four other ponies not included in this series died of the treatment. One relapsed and was treated with atoxyl, orpiment and tartar emetic for fifteen days and was stated to be cured. Six other ponies were treated with a combination of atoxyl and tartar emetic plus orpiment and sodium arsenate. In three of this series the results were not successful. A number of animals showed relapses before they were cured. The doses of orpiment employed were much smaller than those recommended by Laveran and Thiroux, who administered up to 30 grams. The maximum dose employed by Holmes was 3 grams of commercial arsenious sulphide of a light yellow color. S. H. Gaiger has reported on the treatment of camel surra with red and yellow orpiment. The results were entirely unsatisfactory. In one camel treated with atoxyl and orpiment the result also was not successful.

TREATMENT WITH TRYPAN RED AND ARSENIC.

In 1905, Laveran first suggested a combination of trypan red and arsenious acid in the treatment of trypanosomiasis. He had obtained good results in mice, rats and monkeys. Franke also strongly recommended the use of trypan red and arsenic for this treatment.

Wendelstadt and Fellner suggested a combination of arsenic and brilliant green and brilliant green and nucleic acid. Magalhaes did not obtain favorable results with sodium arsenate and brilliant green.

Thomas gave up the combined arsenic and dye treatment because of the nephritis and local necrosis so frequently caused by it, although Breinl and he thought that a combination of arsenic and an improved form of trypan red, if it could be obtained, would seem indicated in the further search for a cure of trypanosomiasis.

TREATMENT WITH ATOXYL AND MERCURY.

Moore, Nierenstein and Todd obtained the best results with injections of bichloride of mercury after the parasites had been caused to disappear from the peripheral circulation by treatment with atoxyl. While in small animals the results were favorable, in larger ones the drugs were not sufficiently efficacious to be of practical value.

Plimmer and Thomson found that the combination of atoxyl and succinimide of mercury was most successful. In a later communication, however, their results were not so favorable. Where sufficient doses of the compound of mercury were given, chronic lesions of the kidney and liver were observed.

Moore, Nierenstein and Todd in further experiments with rabbits and donkeys infected with *Trypanosoma gabiense*, used atoxyl and bichloride of mercury. The outcome of this work was, to use the authors' own words, extremely disappointing. It was found impossible to save a single animal. Of 5 rabbits infected with *Trypanosoma brucei* and treated in the same way, 4 were apparently cured. These authors also performed experiments on dogs, guinea pigs and mice with arsacetin (acetylated atoxyl), followed by bichloride of mercury. They considered treatment with arsacetin followed by a compound of mercury more efficacious than treatment by arsacetin alone, and arsacetin of more value than atoxyl, but believed none of these methods to be of practical value since death invariably occurred.

These authors also employed combinations of atoxyl-silver nitrate; atoxyl-lead acetate; atoxyl-quinine cacodylate; atoxyl-potassium bichromate; atoxyl-quinine.

These were found to be valueless. Treatment of mice infected with *Trypanosoma brucei*, with trypan red followed by bichloride of mercury, was superior to trypan red alone, but inferior to the combined treatment with atoxyl and bichloride of mercury.

Laveran and Thiroux also used a combined treatment with atoxyl and bichloride of mercury on guinea pigs infected with the surra parasite. Their results were not particularly favorable, although better than with the treatment by atoxyl alone.

Uhlenhuth, Hübner and Woithe report that in rats the combined treatment was of considerable value.

Gray described a thorough trial of the treatment of sleeping sickness with atoxyl and bichloride of mercury. The results obtained were much superior to those with atoxyl alone, but were far from satisfactory.

Broden and Rodhain found that the combined treatment with atoxyl and bichloride of mercury did not prove itself at all superior to that with atoxyl alone.

Breinl employed acetylated atoxyl, sublimate and Donovan's solution, in 6 monkeys. Five out of the 6 animals were alive and free from parasites at the time the report was made.

Hodges states that the results of the treatment of sleeping sickness with atoxyl and bichloride of mercury do not, at present, promise to be of a more permanent nature than do those with atoxyl alone.

TREATMENT WITH ATOXYL AND ANTIMONY.

Broden and Rodhain, and Martin and Darné, in the treatment of sleeping sickness, combined atoxyl with injections of the soluble antimony compounds with very encouraging results in early cases of the disease.

Hodges states that in man, treatment by atoxyl and antimony has not at present shown favorable results in Uganda, although these remedies in combination and alternation are being more extensively tried.

Rennes treated one horse infected with dourine with atoxyl combined with antimony. Two months afterwards the blood of the animal was free from parasites. Six months after the beginning of the treatment, the horse was apparently well. He was then reinoculated and contracted a new infection.

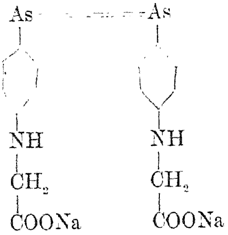
Martin, Leboeuf and Rigenbach believe that atoxyl given with tartar emetic is more poisonous than when given alone, but that the combination is the most effective treatment for trypanosomiasis they have tried. The antimony compound was given intravenously in doses not greater than 10 centigrams of a 1 per cent solution. They treated 31 cases of sleeping sickness with the combination of atoxyl and the antimony compound. Only one of these was in the first stage of the disease. Of the 31, at the time of the report, 10 were dead, 11 had abandoned treatment and 10 were still under observation; 7 of these had parasites in their blood. The authors finally conclude that while the combination of atoxyl and tartar emetic is capable of giving excellent results in early cases, it does not succeed in those which have entered the second stage of the disease.

TREATMENT WITH ARSENOPHENYLGLYCIN.

Through the courtesy of Prof. Paul Ehrlich, of Frankfort, who very kindly offered to send us new preparations made in his laboratory and which seemed of most value in the treatment of trypanosomiasis, for further experimentation in the treatment of larger animals and for a demonstration of their practical efficiency, a shipment of arsacetin was first received and, in the beginning of the year 1909, a shipment of arsenophenylglycin. Professor Ehrlich has continued to supply us with repeated shipments of arsenophenylglycin and all of our experiments with this drug have been carried on with the compound prepared and sent from his laboratory. We take this opportunity of expressing our gratitude to Professor Ehrlich for having given us the opportunity to study carefully the effect of this preparation and for so generously supplying us with the drug.

Arsenophenylglycin is a light yellow powder, very soluble in water and containing about 38 per cent of metallic arsenic (atoxyl contains about 31 per cent).

It has the following formula:



It is considerably less toxic than atoxyl.

The drug was received in sealed glass vacuum tubes. Since it is readily oxidized to a much more toxic, brown substance when exposed to the air, it should be dissolved and used immediately after such exposure. The most favorable strength for injection is from 5 to 10 per cent. It may be given either subcutaneously or intravenously. In man, subcutaneous injection at times calls forth a marked local reaction with subsequent abscess formation. This local reaction is sometimes dependent, according to Ehrlich, upon too strong an alkalinity of the preparation.

Although we now have been experimenting with arsenophenylglycin in the treatment of trypanosomiasis for nearly a year, we have made no previous publication of our results, because we wished to wait until the work had been carried on in sufficient detail and for a sufficient length of time to enable us to draw definite conclusions. A study of the literature of the treatment of trypanosomiasis reveals the fact that many of the publications on this subject have been premature. Remarkable claims have been made in turn for each method of treatment, which have not been borne out by more detailed and extensive experiments carried on for longer periods of time.

Our work with this drug has been confined entirely to monkeys, horses and cattle. In our opinion nothing would be gained by experimenting with smaller animals, since several other methods of treatment had already given satisfactory results in mice and rats, but these had failed to cure the larger animals.

It will be seen from our results with monkeys and horses that arsenophenylglycin is the most nearly ideal drug in the treatment of trypanosomiasis that we as yet possess. While our work with this preparation was in progress, several publications on the value of this drug in the treatment of experimental trypanosomiasis in animals have appeared and these will now be reviewed briefly.

Wendelstadt and Roehl have both shown that a single injection of arsenophenylglycin is capable of curing severe trypanosoma infection in mice and rabbits. Roehl has also demonstrated the prophylactic effect of the drug in these animals.

Schilling and Jaffé also have shown the unquestionable value of arsenophenylglycin in the treatment and cure of mice and rats infected with the nagana trypanosoma, the animals frequently being cured by a single injection of the drug. In their experiments with horses, all of the animals died, apparently from the effect of the drug in the doses employed.

Mesnil and Kerandel inoculated three monkeys infected with *Trypanosoma gubiense* with arsenophenylglycin. In two, the parasites disappeared and had not returned after about three and one-half months. In the third a relapse occurred, then the second injection was given and for the following two and one-half months the animal was free from parasites. They also demonstrated the prophylactic value of the drug in several monkeys and have obtained good results with it in the treatment of four guinea pigs infected with the trypanosoma of Togo.

Eckard has treated 19 cases of sleeping sickness with arsenophenylglycin. Twenty-four hours after the injection, the parasites could no longer be found in the patients' blood. The author was unable to state definitely the value of the drug, owing to the short time which had elapsed between the time the injections were made and the date of the report.

Breinl and Nierenstein report experiments with 20 rats, each of which received the dose of arsenophenylglycin recommended by Roehl, 0.4 gram per kilo or a smaller dose. All died from the effect of the drug. Of 5 guinea pigs infected with trypanosomata and treated, 3 died; 2 from the effects of the drug, and 2 were alive and well after 240 days. Three monkeys were treated with a single dose. Two were alive and well 270 days later. One died from the effects of the drug. Dogs could also be cured of infection by repeated injections, even in advanced cases. Four donkeys and 1 pony were treated with subcutaneous inoculations of the drug. One donkey died after a dose of 0.1 gram per kilo. Another succumbed apparently to the local gangrene caused by the drug. In the other three, large injections did not save the animals which died later of infection. These authors believe that the drug is superior to atoxyl, but that the chance of successful treatment with it diminishes as the size of the animal increases.

Zupitza has employed arsenophenylglycin in 25 cases of sleeping sickness. The treatment appears to be the most favorable which had been attempted at the time the report was made. The parasites disappeared from the blood more quickly after the injection of arsenophenylglycin than after any other drug employed. Relapses had occurred in some of the cases. The time of observation had been too short to draw any more definite conclusions. Twelve horses and 7 donkeys were also treated with this drug. The statement was made that one-half of them had been at work for 5 months after the discovery and treatment of the infection. At present Zupitza's article is not at hand and we have only been able to consult a review. We can not therefore conclude whether these animals were free from trypanosomata and had been cured.

EXPERIMENTS WITH ARSENOPHENYLGLYCIN IN MONKEYS.

Dosage.—One of the first questions which seemed necessary to answer was the dosage of arsenophenylglycin most favorable for the treatment of these animals. Ehrlich had suggested to us about 0.1 gram per kilo of body weight. However, when this amount was injected into normal monkeys, it was found to kill far too high a percentage of the animals for the dose to be practical for treatment. Hence we found it necessary to employ the drug in smaller quantities.

In our preliminary experiments with this preparation, 53 monkeys were employed. Our results were very unsatisfactory, for our animals very frequently died, either from the toxic effects of the drug, or from trypanosomiasis, due to the fact that sufficiently large doses of arsenophenylglycin to cure the infection had not been administered. Later we learned that this first lot which we received was an inferior product in comparison with the drug as prepared by Ehrlich at a later date. For this reason the detailed experiments and the protocols of these 53 monkeys are omitted in this paper. It is believed that their introduction would only cause confusion, as the results obtained are now of little value as compared with those derived from our later and most complete experiments with arsenophenylglycin. Mention here of these preliminary experiments is merely made in case that other observers have encountered similar results with an inferior sample of the drug. A short time after these first experiments were carried out, a second shipment of arsenophenylglycin was received and the fatal dose for monkeys accurately determined with this preparation.

The monkeys employed in these experiments, *Cynomolgus philippinensis* Geoff., were in good condition, having been recently captured. The results in determining the dosage are given in Table I, from which it may be seen that the minimum lethal dose equals 0.22 to 0.26 gram per kilo of body weight of animal. The drug was administered in 5 per cent solution, subcutaneously. No local reaction of any consequence was noted following our injections into monkeys. In using the arsenophenylglycin, the sealed tubes were opened, the drug dissolved at once in distilled water and immediately injected. Those animals which died with acute symptoms from an overdose of the drug usually lived only for from two to ten days after the injection. Some of them suffered with bloody diarrhœa before death. At autopsy, the liver and kidneys usually showed marked fatty degeneration, the lesions present being similar to those which have been regularly described in poisoning from atoxyl.

Treatment.—After determining the most favorable dosage necessary in monkeys, we proceeded to treat animals which had previously been infected with the trypanosoma of surra. In every instance the parasites were present in the blood of the animal at the time the treatment was undertaken.

Discussion of Table II.—Table II gives the results observed with four series of monkeys, the individuals of a given series having been inoculated with the same surra blood at the same time and treated at the same interval after the infection.

SERIES I contains 20 monkeys, 10 of which had been recently captured, the others having been in captivity in the laboratory for variable periods of time. Many of the latter had been used for other experiments and were not in good condition at the time of the present inoculation. For this reason both sickly and robust monkeys were arranged in each group, receiving the same dose of the drug. The strain of trypanosoma employed for inoculating the monkeys of this series was a virulent one, originally obtained from a native pony which showed well-marked symptoms of surra; it had been passed successively through 2 horses, 1 monkey, and then through a third horse before being employed in these experiments. No attempt was made to treat any of these "passage" animals until after the strain of surra had been passed to the next host, and hence the trypanosomata, when inoculated into the monkeys of this series, had never been in contact with arsenic.

About 3 cubic centimeters of the blood of the last "passage" horse, in which the trypanosomata were fairly numerous, were suspended in 100 cubic centimeters of salt solution, and 2 cubic centimeters of the suspension were inoculated subcutaneously into each of the 20 monkeys on July 8, 1909. On July 12, 1909, a blood examination proved to be positive in nearly every instance, and on July 13, when the treatment was begun, trypanosomata were present in the blood of all the monkeys, being very numerous in most instances.

Two of the monkeys of the series were left untreated to serve as controls, and these died, one seventeen and the other fourteen days after inoculation. Monkey No. 4293, which had been in captivity at the laboratory for a long time, was found dead on the third day after inoculation.

The arsenophenylglycin was administered subcutaneously in doses varying from 0.04 to 0.09 gram per kilo of body weight. Monkeys Nos. 4332 and 4341 were animals which had been employed previously for other experiments and were in poor condition at the time of the present experiment; the former died in eight days, the latter in five days after the treatment, death being due, in our opinion, to the combined effect of exhaustion from prolonged captivity and the surra infection and to the toxic effect of the drug. The results obtained with these 2 monkeys should be disregarded.

With these exceptions, it is seen from Table II that every monkey receiving an injection of 0.06 gram per kilo or less showed a relapse of the infection after an interval of from eighteen to fifty-five days. As soon as they were found to have suffered a relapse, all of the monkeys with the exception of No. 4421, were given a second dose of 0.08 gram of arsenophenylglycin per kilo. With the exception of monkey No. 4473, which died within four days after the second injection, all were, we believe, permanently cured. Two are still alive seven months after the second treatment. Many have become somewhat weak and emaciated from their long confinement in small cages. However, the emaciation was not due to a relapse of the surra infection which remained undiscovered, as was shown by the following observation:

Three of the treated monkeys (Nos. 4479, 4476, and 4481) which were so thin and weak that it was obvious they could live under existing conditions only for a few weeks longer, were taken on November 11, 1909, to the residence of one of us and kept in the open air on a chain. They all quickly began to gain in strength. One died a few weeks later after having been exposed to wind and rain. The other two gained in weight and strength and are still alive.

We believe, therefore, that a number of our monkeys which, although cured, finally died after long periods of captivity, could have been kept alive by placing them under better conditions with regard to food and environment and that this should be kept in mind in studying the tables. Monkey No. 4432, although still free from parasites, was losing in weight and strength and, in view of the possible existence of a latent infection with surra, on October 12 a dose of 0.15 gram per kilo of arsenophenylglycin was administered. This monkey was found dead on the morning of October 22, 1909, its blood having been examined on October 21 with negative results. It seems extremely probable that if the third treatment had been omitted and this monkey had been placed under more favorable conditions, it would not have succumbed.

Of the monkeys receiving 0.07, 0.08, and 0.09 gram per kilo, some were permanently cured by the single inoculation, while others suffered a relapse and were treated a second time with a larger dose. Four of these monkeys have remained free from trypanosomata for eight and two-thirds months after a single treatment with the drug.

A summary of the experiments of Series I shows that a single injection of 0.04 to 0.06 gram of arsenophenylglycin per kilo of body weight causes a disappearance of the trypanosomata from the peripheral circulation, but that the parasites reappeared after a variable length of time; that a dose of 0.07 to 0.09 may effect a permanent cure or may not, but that the majority of monkeys so treated recover. Furthermore, not a single relapse occurred after the administration of 0.08 gram per kilo as a second treatment.

SERIES II.—The surra trypanosoma employed in this series was obtained from a native pony that had acquired the infection under natural conditions. An American horse was inoculated subcutaneously with the blood of this pony and six days later his blood was used for the inoculation of the monkeys. On August 4, 1909, 1 cubic centimeter of the horse's blood was suspended in 20 cubic centimeters of salt solution and 2 cubic centimeters of the suspension given subcutaneously to each of the 8 monkeys. The untreated control monkey died of the infection twenty-six days after the inoculation. The other monkeys were treated on August 10, 1909, and all were given a dose of 0.08 gram of arsenophenylglycin per kilo; only one of these (No. 4559) was definitely shown to have suffered a relapse. One animal, No. 4561, received only a single injection of the drug and is still alive, seven months after the treatment. The majority of the other monkeys were given a second treatment with a larger dose (0.1 to 0.15 gram per kilo); one of these is still alive, the others, apparently on account of their weakened condition, succumbed to the toxic effects of the drug.

Monkey No. 4565 was free from trypanosomata November 16 (three and one-half months after treatment); it has since escaped.

The experiments of Series II indicate that the majority of the monkeys treated with a dose of 0.08 gram per kilo will recover from trypanosomiasis, and, hence, the results obtained in Series I are confirmed.

SERIES III.—The strain of surra employed in these investigations was obtained from one of the horses on the Government stock farm at Alabang where an epidemic of surra existed. From this horse the strain was inoculated into a monkey. On September 9, 1909, 1 cubic centimeter of the monkey's blood containing numerous trypanosomata was added to 200 cubic centimeters of salt solution and 1½ cubic centimeters of the suspension injected into each of 21 monkeys.

Two of the untreated monkeys which served as controls died twenty-two and twenty-three days, respectively, after the inoculation with surra blood. A third monkey, No. 4630, was already moribund from the infection at the time when the treatment of the other monkeys was begun, and may therefore be regarded as a third untreated control.

On September 14 trypanosomata were found in the blood of all the monkeys of the series and treatment in doses of 0.1 to 0.26 gram per kilo, of arsenophenylglycin was administered. None of these monkeys have suffered a relapse and none have received a second treatment. Eleven of them are alive and free from trypanosomata, after five and two-thirds months.

One (monkey No. 4616) was free from parasites for four and one-half months and was then lost. Monkey No. 4625 died after three months, its blood being free from parasites just before death. The other animals of the series which died, apparently succumbed from the effects of the drug.

Series III demonstrates clearly that monkeys receiving single doses of from 0.1 to 0.26 gram of arsenophenylglycin are permanently cured of the disease, although some of them will die from the toxic effects of the drug. Doses of from 0.1 to 0.2, inclusive, effect permanent cures with only a small percentage of deaths.

SERIES IV.—On September 22, 1909, the monkeys of Series IV were inoculated with the blood of monkey No. 4632, which constituted a control animal employed in Series III. Trypanosomata were found present in the blood of these animals on September 27 and all but one, which served as a control, were treated on September 28. The untreated control monkey died from the surra infection seventeen days after inoculation.

Very large doses of the drug (0.26 to 0.36) were administered and the three animals which survived these doses have remained free from parasites for six months.

Summarizing these results, it may be stated that not a single monkey which received 0.1 gram of arsenophenylglycin per kilo or a greater amount has shown trypanosomata in the blood twenty-four hours after treatment was given and at no time subsequently have the parasites reappeared. From Table I it is seen that the minimum lethal dose is from 0.22 to 0.26 gram, which is more than twice the dose shown to be efficacious in producing a cure in monkeys.

These experiments, therefore, show conclusively that monkeys, *Cynomolgus philippinensis* Geoff., can be cured permanently of surra infection by a single injection of arsenophenylglycin.

EXPERIMENTS IN HORSES.

Early in the year 1909 attempts were made to treat horses infected with surra and brought to the laboratory. The animals were placed in a small screened stable where they were not kept under the best hygienic conditions. Here their weight could only be estimated approximately, and hence the dosage of the drug administered could not be properly controlled. Many of the horses died from the toxic effect of the drug; others during the course of the treatment suffered a relapse of the infection and were either killed or succumbed during further treatment. In some instances a relapse occurred after the animal had survived a large initial dose. The repeated administration of small doses of arsenophenylglycin gave very unsatisfactory results. None of these animals survived. Later we were able to obtain the weight of 5 horses before beginning treatment, with these the results were as follows:

Weight of horse.	Dose in grams per kilo.	Remarks.
460 kilos	0.05	Recovered from effects of drug.
580 kilos	.052	Died in 8 days.
521 kilos	.058	Recovered.
430 kilos	.065	Died suddenly 24 days later.
371 kilos	.066	Died in 2 days.

From these preliminary experiments it appears that the minimum lethal dose for a large American horse is about 0.052 gram per kilo. A horse which died after receiving this amount per kilo was a very fat animal which had been foundered, so that the dose was actually relatively higher than the figures indicate.

Our experiments indicate, therefore, that the minimum lethal dose per kilo of body weight is about three times as great for monkeys as it is for horses.

Moore offers the following explanation for the discrepancies in dosage between large and small animals when calculated on the basis of the body weight. He emphasizes the fact that the seat of biochemical activity after the administration of arsenic or antimony is in the intestinal mucosa and that it would seem probable that this is also the seat of manufacture of the trypanocidal substance. In the larger animals the therapeutic dose is therefore lowered because of the relatively smaller number of the intestinal cells to take up the drug and the consequent rapid poisoning of the animal if the attempt be made to give the relative dose. The relatively small number of cells must first act upon the drug before it can be turned out as a trypanocide for the parasites.

This hypothesis can hardly be considered tenable without further experimental evidence. According to Moore's theory, the maximum dose is proportional not to the body weight but to the two-thirds power of the body weight.

Following are the details of the earlier experiments carried on with horses:

Horse No. 1.—Native pony. No history as to length of time sick with surra. Head droops and general appearance bad, respirations rapid. Slight œdema of abdomen, mucous membranes of mouth and tongue pale. Examination of blood on April 22 with one-twelfth oil immersion shows about 1 trypanosoma to a field.

April 24, 4.8 grams of arsenophenylglycin dissolved in 100 cubic centimeters of distilled water and injected subcutaneously.

April 25, blood examination for trypanosomata negative.

April 29, second injection of 6 grams of arsenophenylglycin subcutaneously.

May 3, third injection of 6 grams of the same drug intravenously.

May 3, just before the injection of the drug, a monkey was inoculated with 20 cubic centimeters of the blood of the horse. Repeated examination of the blood of the monkey never revealed trypanosomata.

May 12, 10 cubic centimeters of horse's blood were injected subcutaneously into a monkey. This monkey's blood was examined at intervals for a month with negative results. However, the horse grew weaker, and was found dead on the morning of May 18.

Although we were unable to demonstrate any trypanosomata in the blood of this animal, nevertheless, we believe that it succumbed from the effects of surra. This was the first animal treated by us, and the doses administered were evidently entirely too small for a cure to result.

Horse No. 2.—April 23. This animal was injected with 20 cubic centimeters of the blood from horse No. 1 and which contained trypanosomata. The animal died on May 11 of surra, being untreated and used for the purpose of keeping at hand a virulent strain of trypanosoma for the infection of other animals.

Horse No. 3.—Native horse; suffered with advanced symptoms of surra. Marked œdema of the abdomen. Numerous trypanosomata present in the blood.

April 24, 4.8 grams of arsenophenylglycin given subcutaneously.

April 25, blood examination negative for parasites. Parasites did not reappear in the blood.

April 29, 2 monkeys inoculated with the blood of this horse. Trypanosomata did not subsequently develop in the blood of either of them. A second subcutaneous injection of 4.5 grams of arsenophenylglycin was given and on May 3 another injection of 10 grams intravenously. On May 3, 1 monkey and May 7, 2 other monkeys were also inoculated with the blood of the horse. All these animals remained negative for trypanosomata for over two months. The horse died six days later (May 9), notwithstanding the fact that no trypanosomata were found in its blood. Nevertheless, this animal probably died of surra infection and from the toxic effect of the last dose of the drug.

Horse No. 4.—Large native horse; received on April 29. Blood examination positive for trypanosomata. No record of how long the animal has been sick with surra. Temperature 40°. April 29, 8 grams of arsenophenylglycin injected subcutaneously. Considerable œdema at the site of the injection on the following day.

May 3, monkey was inoculated with 30 cubic centimeters of the blood of the horse, but no trypanosomata developed in its blood. Following the inoculation of the monkey 15 grams of the drug were given intravenously to the horse, although the blood examination the previous day had been negative for parasites.

May 12, a second monkey was inoculated in the same manner with the same result.

June 4, a third monkey was inoculated with 20 cubic centimeters of the horse's blood, on the 15th of June it developed trypanosomiasis and died on the 26th.

This experiment demonstrates that this strain of trypanosoma had not lost its virulence, although the animal from which it was taken had received previously 2 doses of arsenophenylglycin.

June 10, an examination of the horse's blood showed a few trypanosomata. On the same day another inoculation of 10 grams of arsenophenylglycin was given intravenously. The parasites disappeared from the blood, but reappeared on July 6 when 11.4 grams of arsenophenylglycin were again given intravenously. Although the trypanosomata did not reappear in the blood, there was given on July 15 another dose of 10 grams of arsenophenylglycin intravenously and on August 3, 11 grams more. Thirty cubic centimeters of the blood of the horse were injected into a monkey on August 3 before the inoculation with the drug. The animal later developed trypanosomiasis. On August 5 the horse was unable to rise and on August 6 he died, evidently succumbing to the surra infection. Although this animal was treated in a screened stable, nevertheless it was necessary to place him alongside another animal which had surra and which remained untreated. It is possible, therefore, that he may have been reinfected with trypanosomiasis from the other surra animal.

Horse No. 5.—Small bay horse; contracted surra naturally. At the time of treatment, April 29, there was œdema of the abdomen and trypanosomata were numerous in the blood. Ten grams of arsenophenylglycin were injected subcutaneously. On the following day there was considerable œdema at the site of the inoculation. On the day following the injection there was watery diarrhœa which lasted about twenty-four hours. Although no trypanosomata reappeared in his blood, he was given a second inoculation of 10 grams intravenously on May 3. Following this, the animal was unable to stand and there was marked tremor of the muscles. The animal died on May 8, evidently of arsenic poisoning. Three monkeys were inoculated with his blood, 1 on May 3 with 20 cubic centimeters, 1 on May 7 with 10 cubic centimeters, and 1 on May 7 with 2 cubic centimeters. None of these animals developed surra infection.

Horse No. 6.—Native pony; contracted surra naturally. The duration of the disease unknown, although the condition of the animal appeared to be good at the time treatment was begun. On April 30 its blood was positive for trypanosomata and 6 grams of arsenophenylglycin were injected subcutaneously, after which the parasites disappeared from the circulation and did not reappear.

On May 4, 15 grams of the drug were injected intravenously. On this date, previous to the injection of the drug, a monkey was also inoculated subcutaneously with 30 cubic centimeters of the horse's blood. This animal did not develop surra. On May 10 there was considerable œdema along the lower margin of the abdomen. The blood remained negative for trypanosomata. The animal died May 28. The immediate cause of death of this animal is not clear.

Horse No. 7. (Treated with arsacetin.)—Native horse which contracted the disease naturally. Condition good at the time treatment was commenced. No information was obtainable regarding the time the animal had been infected with surra. Blood examination April 30 was positive for trypanosomata. On this date 8 grams of arsacetin were given subcutaneously. The parasites disappeared from the animal's blood and remained absent. On May 5 there was given a second inoculation of 15 grams of arsacetin intravenously. The horse died on the following day of arsenic poisoning. A monkey inoculated on May 6 with 20 cubic centimeters of its blood did not develop surra.

Horse No. 8.—Chinese horse, infected artificially in the laboratory. Inoculated subcutaneously with 10 cubic centimeters of the blood of horse No. 2 just before it died of surra. Horse No. 8 was untreated and died of surra on June 15. On June 4, June 14, and May 17, respectively, monkeys were inoculated with the blood of this horse and all developed surra infection and died in nineteen, and seventeen, and eleven days, respectively, thus demonstrating the virulence of the strain employed in these experiments.

Horse No. 9.—Small native horse; infected naturally with surra. No information regarding the length of time of infection. On May 21 the animal was injected with 10 grams of arsenophenylglycin intravenously. Trypanosomata disappeared from the blood. On June 12 the animal's temperature rose to 39.8° although no parasites could be found in the blood. A monkey was inoculated with 20 cubic centimeters of the blood and on June 22 was found to have trypanosomata in its blood. Because of the rise of temperature on June 12, the horse was given another injection of 10 grams of arsenophenylglycin intravenously. On June 27, the horse was unable to rise, although the blood showed no trypanosomata. On June 28 a monkey was inoculated with 12 cubic centimeters of the horse's blood. This monkey, however, did not develop trypanosomiasis. The horse died on June 30, the temperature being 40°. This animal also probably died of surra infection.

Horse No. 10.—Native horse; contracted the disease naturally. Œdema of the abdomen and scrotum at the time the treatment was begun. No informamation regarding the length of time since the animal contracted the infection. On May 21 it was given an injection of 10 grams of arsenophenylglycin. Trypanosomata disappeared from the blood. On June 7, œdema of the abdomen and scrotum was still present. A monkey was inoculated with 35 cubic centimeters of the blood of this horse and died on June 18 of surra. On June 10, the trypanosomata reappeared in the horse's blood, when 10 grams of arsenophenylglycin were given intravenously. On June 29 another monkey was inoculated with 22 cubic centimeters of the horse's blood. This monkey died later of surra.

On June 29 the horse was given 10 grams of arsenophenylglycin subcutaneously and on July 14 he was unable to rise. On July 16 the horse was killed. The examination of the blood and organs were negative for trypanosomata. This animal probably also had surra infection when it was killed.

Horse No. 11.—Native pony; contracted the disease naturally. No information as to length of time the animal had been infected. Œdema of the abdomen and other symptoms of surra present. This animal was not treated and died on June 1 of surra, the animal being used for control purposes.

Horse No. 12.—Arrived in the advanced stages of surra. The animal was killed on May 12, but no trypanosomata were found in the spleen, bone marrow, lymphatic glands, or blood. Fluid from the lateral ventricle of the brain was collected and centrifugated. A few trypanosomata were found in the sediment.

Horse No 13.—Large American horse; infected artificially with 1 cubic centimeter of the blood of a monkey infected with surra. This monkey had been infected six days previously with the blood of horse No. 8. Five days later the blood of the horse showed numerous trypanosomata. This animal was untreated and died of surra on July 14, less than one month from the date of its infection.

The course of the disease in this animal proved the virulence of the strain employed in the further experiments.

Horse No. 14.—American horse (weight 431 kilos); infected artificially on July 12 by subcutaneous injection of 10 cubic centimeters of the blood of horse No. 13. July 21 numerous trypanosomata were present in the animal's blood. On July 22 an injection of 28 grams of arsenophenylglycin in 300 cubic centimeters of salt solution was given intravenously (0.065 gram per kilo). The trypanosomata disappeared from the blood and did not reappear. The animal was found dead on August 15. The cause of death in this instance is obscure, but was probably due to the toxic effect of the drug. The horse died quite suddenly, having appeared to be in good condition on the previous day, when he suddenly fell to the ground.

Horse No. 15.—American horse (weight 375 kilos); infected artificially with 2 cubic centimeters of the blood of horse No. 14, containing numerous trypanosomata. Five days later parasites were present in the blood of the animal and the following day they were numerous. On this date the animal was given 25 grams of arsenophenylglycin intravenously (0.066 gram per kilo). On July 29, two days later, this animal died of arsenic poisoning.

Horse No. 16.—American horse (weight 502 kilos); infected with 2 cubic centimeters of the blood of horse No. 14 on July 22. On July 26 the blood of this animal was positive for trypanosomata. On July 29, 11.5 grams of arsenophenylglycin were injected intravenously (0.05 gram per kilo). The parasites were absent from the blood of the animal on August 3. Although the blood was negative for parasites, the animal appeared sick and did not eat well. For this reason a second injection of 10 grams of arsenophenylglycin was given intravenously. Following this injection the horse suddenly became weak, staggered and fell to the ground. The animal died on August 9 of arsenic poisoning.

Horse No. 17.—American horse (weight 460.4 kilos); infected with 2 cubic centimeters of the blood of horse No. 16 on July 29. On August 2, blood positive for trypanosomata. On August 7, 23 grams of arsenophenylglycin were injected intravenously (0.05 gram per kilo). The trypanosomata disappeared from the blood and remained absent until August 30. On August 30 the blood was positive for trypanosomata and the animal was killed.

Horse No. 18.—American horse (weight 466.8 kilos); infected artificially with 5 cubic centimeters of the blood of horse No. 17. On August 10 trypanosomata were present in the blood of this animal and it was treated with 1,250 cubic centimeters of 0.5 per cent potassium antimonyl tartrate to which hydrogen sulphide had been added and then carbon dioxide had been passed through the solution to remove the excess of hydrogen sulphide. The trypanosomata disappeared from the blood and remained absent for fifteen days when they again reappeared in large numbers. On the same day 1,500 cubic centimeters of the same solution were injected. The animal was found dead on the following day, death being due to antimony poisoning.

Horse No. 19.—Native horse admitted on October 18, having acquired the surra infection naturally. Numerous trypanosomata were present in the blood. On October 27, when the disease was well advanced the animal was killed. On October 19, 5 cubic centimeters of this animal's blood, which contained numerous trypanosomata, were injected into horse No. 20.

Horse No. 20.—Infected with 5 cubic centimeters of the blood of horse No. 19. On October 27 trypanosomata were numerous in the blood, when 30 grams of arsenophenylglycin were injected intravenously (0.052 gram per kilo). Following the inoculation the parasites disappeared from the circulation. Although the animal's condition appeared good, after the injection diarrhœa developed and the animal was found dead on the morning of November 4, evidently having succumbed to arsenic poisoning.

Horse No. 21.—American horse (weight 521 kilos): injected with 5 cubic centimeters of the blood of horse No. 19 on October 19. October 27 positive for trypanosomata. Thirty grams of arsenophenylglycin were given by subcutaneous and intravenous injection (0.058 gram per kilo). There was profuse perspiration following the injection and the animal became very restless. On November 6 a considerable area of induration appeared just above the front shoulders of the horse. This was incised but no pus was present. On November 12, 10 cubic centimeters of the blood of the horse were injected into a monkey. This monkey later developed surra on November 19, from which it died on November 24. On November 12, although the condition of the animal appeared good, 20 grams of arsenophenylglycin were again injected intravenously. On November 29, although the blood of the horse was negative for parasites by microscopical examination, a second monkey was inoculated with its blood. This animal developed surra infection on December 6. On November 29. the horse was given 19 grams of arsenophenylglycin intravenously. On December 7 the blood of the horse was again injected into another monkey. This animal remained negative for parasites. December 7 the horse was given another injection of 20 grams of arsenophenylglycin intravenously.

On January 3 the temperature registered 40°. An examination of the blood showed a few trypanosomata present. Twenty-five grams of the drug were then given intravenously. The parasites then disappeared from the blood and were not found present on repeated examinations up to January 20. On January 19 the condition of the horse appeared to be good. On January 20, although his temperature was normal, he refused to eat and became unable to rise and died a few hours later. The autopsy showed advanced glomerular nephritis, cloudy swelling of the liver and heart muscle. The large intestine was greatly distended with gas. The spleen was somewhat soft and friable. Microscopic examination of the blood was negative after repeated examinations. The cerebral fluid from the ventricles and the spinal fluid were centrifugated and one trypanosoma was found in each of three smears made from the sediment. A monkey was then inoculated with some of the blood and later developed surra.

The treatment of this horse demonstrates very forcibly the inefficiency of the drug in some instances. This animal had received five intravenous injections of arsenophenylglycin in amounts of 30, 20, 19, 20 and 25 grams. Notwithstanding the fact that at autopsy marked lesions due to arsenic poisoning were present, nevertheless a few trypanosomata had resisted the action of the drug and these were active and proved capable of causing infection and death in another animal. Furthermore, the treatment was begun in this horse eight days after infection.

Horse No. 25.—American horse, brought to laboratory on February 1 for treatment for surra. At the time of its arrival the disease was evidently well advanced. A blood examination showed the presence of trypanosomata and of microfilariæ. Nineteen grams of arsenophenylglycin were injected intravenously. On the following day there was considerable swelling about the point of the injection. The animal gradually grew worse, the œdema increased, and it died on February 15. Three days before its death there was considerable fever, but the blood was negative for trypanosomata.

Mule (American) No. 26.—This animal was observed in the Province of Bulacan. The blood was examined on December 19 and trypanosomata found therein.

On this date 19 grams of arsenophenylglycin were injected intravenously. The animal was brought to Manila two days later. At this time there were no evident symptoms of surra. On December 27, 20 grams of arsenophenylglycin were again injected intravenously. On January 6, 23 grams of the drug were given intravenously. The blood remained negative, although almost daily examinations of it were performed, until February 2, when a few trypanosomata were found present. On February 2, 25 grams of arsenophenylglycin were injected intravenously. A monkey was inoculated on this date with the blood of this mule and it later developed surra. The mule died on February 9, the treatment having evidently proved unsuccessful.

Surra in Bulacan Province.—A small outbreak of surra recently occurred in Bulacan Province, near Manila, and a few of the infected animals were treated there. The treated animals were all kept and worked together. Consequently, when a relapse of the infection occurred in one of them the others were exposed. It was practicable to visit the animals for examination and treatment only once a week. Owing to the favorable results that had been reported by Holmes in India from the treatment of trypanosomiasis in horses by a combination of atoxyl and orpiment, we determined to give this method, also, a trial in these animals. Seven mules and 3 horses were treated in a somewhat similar manner, as may be seen from the notes of the experiments which follow. In some instances arsacetin or arsenophenylglycin was substituted for the atoxyl.

Five mules were given alternate doses of atoxyl and orpiment, the atoxyl being given subcutaneously and the orpiment (arsenic trisulphide) by mouth. In all but one of these, relapses occurred shortly after the treatment was stopped, and we deemed it advisable to substitute arsenophenylglycin for this method of treatment. The details of these experiments are as follows:

Horse No. 22.—Native horse; contracted surra naturally. Length of time infected unknown. Numerous trypanosomata in the blood at the time of entrance. On December 4, 5 grams of arsacetin were given subcutaneously. On December 5 no trypanosomata were found. On December 10, 10 grams of arsenic sulphide were administered by mouth. Following this, the horse became unable to rise and died of arsenic poisoning on December 8. The arsenic sulphide used in this case was precipitated and was not thoroughly washed with alcohol or ether and probably contained a percentage of white arsenic.

Horse No. 23.—American horse infected with 5 cubic centimeters of the blood of horse No. 22 on December 3. On December 7 its blood was positive for trypanosomata. The parasites became numerous on December 9, on which date 15 grams of arsenic sulphide were administered in capsule by mouth. On December 10 the parasites were still numerous; December 11, only one trypanosoma was found in a drop of fresh blood. On the same date 5 grams of arsacetin were injected subcutaneously. On December 13 another dose of 10 grams of arsenic sulphide was given. December 16, 5 grams of atoxyl; December 23, 10 grams of arsenic sulphide; December 27, 5 grams of atoxyl; January 2, 20 grams of arsenic sulphide; January 5, 5 grams of atoxyl; January 9, 20 grams of arsenic sulphide; January 13, 5 grams of atoxyl; January 17, 25 grams of arsenic sulphide.

This animal is apparently well. Repeated examinations of its blood and inoculations of it into 3 monkeys have been made. None of the animals have developed trypanosomiasis.

Horse No. 24.—American colt infected artificially with 5 cubic centimeters of the blood of horse No. 22 on December 4. December 7 blood examination showed a few trypanosomata. December 9, trypanosomata numerous, when 10 grams of arsenic sulphide were administered by the mouth in capsules. December 10, trypanosomata numerous; December 11, 5 grams of arsacetin injected subcutaneously. From December 11 to December 17 the horse was given alternate doses of arsenic sulphide and arsacetin and died on December 18 of arsenic poisoning.

Mule (American) No. 27.—This animal was also examined at Bulacan on December 17 and trypanosomata found in its blood. On the same date 15 grams of arsenic sulphide were given by mouth. December 19 the blood was still positive for parasites and 15 grams of arsenophenylglycin were injected intravenously. The animal was brought to the laboratory on December 21. Its temperature on examination was 40° and there was considerable œdema between the front shoulders. The temperature dropped to normal on December 24, although the marked œdema increased along the whole of the abdomen. December 27, 20 grams of arsenophenylglycin were given intravenously, although the blood remained negative for parasites. Twenty-five grams of the drug were again given on January 4 and 25 grams on January 25. A monkey was inoculated on January 25 just before the injection of the drug and did not develop surra infection. On February 14, 10 grams of arsenic sulphide were given the animal by the mouth, through a mistake on the part of the attendant. On March 23 trypanosomata reappeared in his blood and he was given 30 grams of arsenophenylglycin.

This animal is at present alive and its blood contains no trypanosomata. It seems not unlikely that this animal was reinfected with surra from another mule which was suffering with the disease and which was kept with it.

Mule (American) No. 28.—This mule was found positive for trypanosomata in Bulacan on December 17. On December 19, 15 grams of arsenophenylglycin were injected intravenously. Shortly after this injection the temperature which had been elevated became normal. On December 27, 15 grams of arsenophenylglycin were given intravenously. The blood remained negative until January 8, when trypanosomata reappeared. The animal was then inoculated with 5 grams of atoxyl, but did not bear the inoculation well and three days later was in a very weak condition. On January 14 the blood examination showed no parasites. On January 22, 24, and 26, 10 grams of arsenic sulphide were given by mouth and on January 29, 5 grams of atoxyl subcutaneously. On January 31, 20 grams of arsenic sulphide; February 2, 30 grams of arsenic sulphide; February 5, 5 grams of atoxyl; February 7, 20 grams of arsenic sulphide; February 9, 20 grams of arsenic sulphide. February 14 the animal became still weaker. He developed pressure sores, and on March 19 trypanosomata reappeared in his blood and he was destroyed.

Mule (American) No. 29.—This animal was also observed at Bulacan. It appeared in excellent condition at the time the trypanosomata were found on December 17, on which date 15 grams of arsenic sulphide were given by mouth. Decembr 19 the blood was still positive for parasites and 5 grams of atoxyl were injected subcutaneously. December 21, 20 grams of arsenic sulphide were given.

December 23 the blood was negative for parasites and 5 grams of atoxyl were injected; December 25, 30 grams of arsenic sulphide; December 28, 5 grams of atoxyl; January 1, 15 grams of arsenic sulphide. January 4 trypanosomata reappeared in the blood and 5 grams of atoxyl were given; January 6, 20 grams of arsenic sulphide; January 8, 5 grams of atoxyl; January 10, 20 grams of arsenic sulphide; January 14, 5 grams of atoxyl; January 18, 20 grams of arsenic sulphide; January 22, 5 grams of atoxyl; January 24, 20 grams of arsenic sulphide; January 26, 20 grams of arsenic sulphide; January 29, 5 grams of atoxyl; January 31, 20 grams of arsenic sulphide; February 3, 20 grams arsenic sulphide; February 5, 5 grams of atoxyl; February 7, 20 grams of arsenic sulphide; February 9, 20 grams arsenic sulphide. February 14, although the condition of the animal appeared good, trypanosomata reappeared in the blood. February 14, 5 grams of atoxyl; February 17, 25 grams arsenic sulphide; February 19, 25 grams of arsenophenylglycin. Since this date the animal has been negative for trypanosomata and is in good condition.

Mule (American) No. 30.—Observed at Bulacan December 17. Examination of the blood positive for trypanosomata. Fifteen grams of arsenic sulphide given by mouth; December 19, 5 grams of atoxyl; December 21, 20 grams arsenic sulphide; December 23, 5 grams atoxyl; December 25, 20 grams arsenic sulphide; December 28, 5 grams of atoxyl. December 30 the animal suffered from diarrhœa and no treatment was given; January 4, 15 grams of arsenic sulphide. January 8 trypanosomata reappeared in the blood. The animal was given 5 grams of atoxyl; January 12, 20 grams arsenic sulphide. Diarrhœa and colic developed. January 14, 5 grams of atoxyl; January 18, 20 grams arsenic sulphide; January 22, 5 grams atoxyl; January 24, 20 grams arsenic sulphide; January 26, 20 grams arsenic sulphide; January 29, 5 grams atoxyl; January 31, 20 grams arsenic sulphide; February 3, 20 grams arsenic sulphide; February 5, 5 grams of atoxyl; February 7, 20 grams arsenic sulphide; February 9, 20 grams arsenic sulphide; February 14, 5 grams atoxyl; February 17, 20 grams arsenic sulphide; February 19, 20 grams arsenophenylglycin. March 23 trypanosomata reappeared in the blood, when 25 grams of arsenophenylglycin were injected intravenously. The animal is still alive and free from parasites.

Mule (American) No. 31.—Found positive for surra on microscopic examination on December 23 at Bulacan. December 23, 5 grams of atoxyl; December 25, 20 grams arsenic sulphide; December 28, 5 grams atoxyl; December 30, 25 grams arsenic sulphide; January 1, 5 grams of atoxyl; January 4, 20 grams of arsenic sulphide; January 6, 20 grams of arsenic sulphide; January 8, 5 grams atoxyl; January 10, 20 grams arsenic sulphide; January 12, 20 grams arsenic sulphide; January 14, 5 grams atoxyl; January 17, 20 grams arsenic sulphide; January 22, 5 grams atoxyl. The animal having been treated about one month, treatment was discontinued until February 14. During this time the blood was negative. February 14, the blood was found positive for trypanosomata, when 5 grams of atoxyl were given; February 17, 20 grams arsenic sulphide; February 19, 20 grams arsenophenylglycin. The blood has since been negative.

Mule No. 32.—American mule found positive for surra by microscopic examination on December 19 at Bulacan, when 5 grams of atoxyl were given; December 21, 20 grams of arsenic sulphide; December 23, blood positive, 5 grams of atoxyl; December 25, 20 grams arsenic sulphide; December 28, 5 grams of atoxyl; December 30, 5 grams atoxyl; January 1, 20 grams arsenic sulphide; January 4, 5 grams atoxyl; January 6, 20 grams arsenic sulphide; January 8, 5 grams atoxyl; January 10, 20 grams arsenic sulphide; January 12, 20 grams arsenic sulphide; January 14, 5 grams atoxyl; January 17, 20 grams arsenic sulphide; January 22, 5 grams atoxyl. Treatment was then stopped, the animal having been treated for one month. On March 5, trypanosomata reappeared in the blood. March 9, 24 grams of arsenophenylglycin were given intravenously. The animal died four days later.

Mule (American) No. 33.—Found positive for surra on December 28 at Bulacan. Arsenic sulphide 20 grams by mouth. December 30, blood negative, arsenic sulphide 20 grams. Animal found dead on morning of January 1.

Epidemic at Alabang.—During the past year an epidemic of surra was also observed among the horses of the Government stock farm at Alabang. On September 3 we visited Alabang and found 17 horses infected with surra. The blood in each instance was examined and the trypanosomata found therein. In many of the animals the parasites were very numerous and the horses showed well-marked symptoms of surra. In the following few weeks 3 other horses were found infected with surra at Alabang and these were treated with the others. The horses, during the course of their treatment, were kept in an open field at one corner of the farm and were fed under a *nipa* roof, which afforded some protection from the sun. Flies were abundant, to the bites of which the horses were naturally exposed. The conditions, therefore, were such as might be met with in combating the disease in provincial districts with no protection against reinfection, either from biting flies or from contact with other infected animals.

Therefore, the conditions surrounding the experiment seemed most unfavorable for obtaining good results from treatment.

The injections of arsenophenylglycin were given intravenously in approximately 10 per cent solution. Since no facilities were at hand for holding the horses while they were being treated, it frequently happened that during the inoculation the needle escaped from the vein so that some of the solution was given subcutaneously. When this occurred, severe local reaction sometimes followed which resulted in abscess formation. However, the abcesses healed later without trouble. No animals apparently died from the local effect of the drug. Owing to the conditions just described, it was impossible in the course of the experiments to determine whether a reappearance of the trypanosomata in the blood of individual horses indicated a relapse, or a reinfection. The experiments in monkeys indicated that a single large dose of the drug gave the best results. However, owing to the fact that some of our horses would almost certainly have been reinfected with surra during the period following the first treatment, we felt compelled to repeat the dose at intervals, even though the blood remained negative in most of the cases. Our experiments with horses have shown us that as few injections as possible should be made, owing to the danger of the production by the drug of grave lesions in the internal organs. Table III gives the results of the treatment of these horses.

Discussion of Table III.—During the few weeks following the first treatment of the horses, trypanosomata reappeared in the blood of a number of them, and since we did not have a sufficient quantity of arsenophenylglycin on hand to continue the treatment of all of the animals, some were destroyed. A few other horses died from the toxic effects of the drug. There remained, then, on November 19 only 8 horses alive. Four of these were brought to Manila and placed in screened stalls. These latter have all remained entirely free from parasites for six months [2] and are in excellent condition at the present time. The blood of these horses has been subjected to repeated examination and as large an amount as 20 cubic centimeters has been repeatedly inoculated at intervals into monkeys with negative results.

One of the horses, No. 73, had a slight rise in temperature on December 13; fearing a relapse, this horse's blood was at once injected into a monkey and the horse was then given a full dose of arsenophenylglycin. The monkey, however, remained free from trypanosomata, and we feel justified in concluding that the rise in temperature was due to some other cause than trypanosomiasis. These horses, we believe, have been cured of surra. One of them has been kept at work for over a month at Manila. Of the other horses, 2 have shown a reappearance of trypanosomata in the peripheral blood after having been free from parasites for three months and five months, respectively. In view of the fact that the horses which were brought to Manila and kept in screened stalls have not shown any relapses, and, also, because the 4 horses left at Alabang remained in the same corner of the farm where the horses infected with surra were originally segregated, it seems not unlikely that the reappearance of the trypanosomata in the two instances just cited resulted from a reinfection from biting insects and was not due to a relapse of the original infection. However, it is possible that a relapse may have occurred. Both of these horses were subjected to further treatment; one succumbed a day or so after the administration of a large dose of arsenophenylglycin, the other is still alive and in good condition three months after the last treatment.

The other horses at Alabang, although negative for trypanosomata, were treated on November 19 as a prophylactic measure because of their intimate contact with the horse showing trypanosomata in its blood. They have remained negative for trypanosomata and are in excellent condition at the present time. They have not been under daily observation, as have the horses that were brought to Manila, but we are inclined to regard them as free from the disease.

We believe, then, that we have on hand 7 horses, all in good condition, which have been definitely and permanently cured of surra by the intravenous administration of arsenophenylglycin.

Surra runs a very chronic course in cattle in the Philippine Islands, the animals harboring the parasites over long periods of time, during which their general health may remain unimpaired. This renders it extremely difficult to determine whether or not a drug used in the treatment of these animals is efficacious. Therefore, although we have treated a number of bullocks that were infected with the disease, we prefer to express no opinion at this time with regard to the action of the drug on these animals.

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[2] At the time of the reading of this proof, now 9 months.

SUMMARY.

In the use of arsenophenylglycin two methods of treatment may be considered, as already outlined by Ehrlich: First, that by stages in which relatively small doses are given and at repeated intervals; second, the treatment by one or several large doses. In monkeys and horses there is no question but that the second method of treatment is the more favorable one. In horses, the most satisfactory results have been obtained where we have given an amount probably very close to the fatal dose to the animal infected. Unfortunately, in horses the margin between the dose necessary to effect a complete cure and the fatal one seems very small (see horse No. 21), too small for us to be able to determine the amount most favorable for any given case. Moreover, the susceptibility of horses to the effect of the drug naturally varies to some extent. The condition under which the animal is kept after treatment, whether favorable or otherwise, may possibly be the deciding point as to whether the animal recovers or dies. Each repetition of a large dose obviously exposes the animal to increased danger of poisoning, while the opportunity of producing a cure is diminished. These facts are evident upon consideration of the action of atoxyl in the human body and from the results of our own experiments.

In conclusion, we do not hesitate to say that arsenophenylglycin has proved to be by far the most satisfactory means of treatment of trypanosomiasis yet discovered. The drug has shown itself to be very efficacious for the treatment and cure of surra infection in monkeys. However, while the results in horses, are the best that have as yet been obtained, they are not nearly as encouraging as in monkeys. We have, however, for the first time been able to cure horses afflicted with surra, and this we never could accomplish before by any other means. While it appears that we can save a certain percentage of the horses infected with surra during an epidemic, we can never predict with certainty whether in a given instance we will be able to cure the horse, or whether he will succumb first to the action of the drug. However, since, the disease is invariably fatal in these animals without treatment, a trial should be made in the case of every horse of any great value. In the epidemic at Alabang, we were able to save a sufficient percentage of the horses to demonstrate that the means is of some practical value in the treatment of surra during an epidemic.

It is not our intention in the present paper to report upon the results we have obtained in the treatment of trypanosomiasis with a large number of other compounds prepared by Doctor Oechslin, of the chemical laboratory of this Bureau. This work is still being continued at the present time, but so far, no results as satisfactory as those with arsenophenylglycin have yet been obtained.

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TABLE I.—*Dosage of arsenophenylglycin in normal monkeys.*

Weight of monkey in grams.	Dose of arsenophenylglycin in grams per kilo.	Death after—	Weight of monkey in grams.	Dose of arsenophenylglycin in grams per kilo.	Death after—	Weight of monkey in grams.	Dose of arsenophenylglycin in grams per kilo.	Death after—
2,250	0.10	----------	2,100	0.18	----------	1,520	0.26	3 days.
1,800	0.10	----------	2,350	0.20	----------	1,440	0.28	----------
2,350	0.12	----------	2,170	0.20	----------	2,170	0.30	3 days.
2,300	0.12	----------	2,820	0.22	----------	2,040	0.30	8 days.
2,300	0.14	----------	2,700	0.22	6 days.	2,370	0.32	3 days.
2,320	0.14	----------	2,620	0.24	----------	1,970	0.32	2 days.
1,900	0.16	----------	2,350	0.24	----------	1,730	0.34	10 days.
2,440	0.16	----------	2,300	0.26	----------	1,750	0.36	2 days.
2,300	0.18	----------	2,400	0.26	3 days.			

TABLE II, SERIES I (Monkeys).

No. of monkey.	Weight in grams.	First treatment in grams per kilo.	Interval between doses.		Second treatment in grams per kilo.	Result.	Period free from trypanosomata.
			Days.	Blood examination.			
4477	2,500	0.04	18	Pos.	0.08	Alive	7 months.
4432	850	0.04	28	Pos.	0.08	----------	2½ months.[a]
4332	1,620	0.04	----------	----------	----------	Died in 8 days (negative)	
4473	3,200	0.05	20	Pos.	0.08	Died in 4 days	
4479	1,100	0.05	34	Pos.	0.08	Died after 3 months	
4341	1,520	0.05	----------	----------	----------	Died 5 days	
4472	5,250	0.06	27	Pos.	0.08	Died in 6⅔ months	
4476	1,950	0.06	19	Pos.	0.08	Alive	7 months.
4421	1,220	0.06	----------	----------	----------	Died in 55 days (positive)	
4293	Died 3 days after inoculation with surra—not treated						
4474	5,900	0.07	----------	----------	----------	Alive	8⅔ months.
4480	1,550	0.07	----------	----------	----------	do	Do.
4337	1,770	0.07	34	Pos.	0.09	Died in 19 days (negative)	
4475	3,950	0.08	----------	----------	----------	Alive	Do.
4481	1,600	0.08	----------	----------	----------	do	Do.
4419	1,200	0.08	23	Pos.	0.10	do	6 months.
4420	750	0.09	51	Pos.	0.10	Died in 3 hours	
4350	1,900	0.09	----------	----------	----------	Died in 17 days (negative)	
4478	2,500	Control—not treated				Died 17 days after inoculation	
4422	850	Control—not treated				Died 14 days after inoculation	

[a] This monkey died 10 days after a third treatment with a dose of 0.15 gram per kilo.

TABLE II. SERIES II (Monkeys).

No. of monkey.	Weight at first treatment.	First dose of arsenophenylglycin in grams per kilo.	Interval between doses.		Second dose of arsenophenylglycin in grams per kilo.	Result.	Period free from trypanosomata.
			Days.	Blood examination.			
4559	1,250	0.08	31	Pos.	0.1	Died in 1 day	
4560		0.08	31	Neg.	0.1	Died in 17 days	
4561	2,700	0.08				Alive	7 months.
4562	1,400	0.02	[a]4	Neg.	0.1	Died in 4 days	
4563	Control—not treated.					Died in 26 days	
4564	2,700	0.08	[a]2	Neg.	0.15	Alive	Do.
4565		0.08				Lost	3½ months.
4566		0.80	[a]4	Neg.	0.15	Died in 2 days	

[a] Months.

TABLE II. SERIES III (Monkeys).

No. of monkey.	Weight at first treatment.	First dose of arsenophenylglycin in grams per kilo.	Result.	Period free from trypanosomata.
4612	2,250	0.1	Alive	5⅔ months.
4613	1,850	0.1	Died in 16 days	
4614	1,700	0.12	Alive	Do.
4615	2,350	0.14	do	Do.
4616	2,200	0.14	Lost	4¼ months.
4617	2,320	0.14	Died in 22 days (negative)	
4618	1,500	0.16	Died in 5 days	
4619	2,450	0.16	Alive	5⅔ months.
4620	2,250	0.18	do	Do.
4621	2,050	0.18	do	Do.
4622	2,300	0.20	do	Do.
4623	2,150	0.20	do	Do.
4624	2,950	0.22	do	Do.
4625	2,000	0.22	Died in 3 months (negative)	
4626	2,170	0.24	Alive	Do.
4627	2,250	0.24	Died in 13 days	
4628	2,000	0.26	Died in 10 days	
4629	2,010	0.26	Alive	Do.
4630	Control—not treated		Died 5 days after inoculation	
4631	Control—not treated		Died 33 days after inoculation	
4632	Control—not treated		Died 22 days after inoculation	

TABLE II, SERIES IV (Monkeys).

No. of monkey.	Weight at first treatment.	First dose of arsenophenylglycin in grams per kilo.	Result.	Period free from trypanosomata.
4655	1,570	0.26	Died in 12 days	
4654	1,450	0.28	Alive	5 months.
4656	2,250	0.30	Died in 1 day	
4657	1,950	0.30	do	
4658	2,150	0.32	Alive	Do.
4659	1,250	0.32	do	Do.
4660	1,700	0.34	Died in 8 days	
4661	1,350	0.36	Died in 1 day	
4653	Control—not treated		Died 17 days after inoculation	

TABLE III (Horses).

No. of horse.	Age.		First treatment.		Interval.		Second treatment.		Interval.		Third treatment.		Interval.		Fourth treatment.		Interval.		Fifth treatment.		Interval.		Sixth treatment.		Entire period free from trypanosomata.	March 5 period since last treatment).
			Date.	Dose.	Days.	Blood examination.[a]	Date.	Dose.	Days.	Blood examination.[a]	Date.	Dose.	Days.	Blood examination.[a]	Date.	Dose.	Days.	Blood examination.[a]	Date.	Dose.	Days.	Blood examination.[a]	Date.	Dose.		
	Y.	m.		G.				G.				G.				G.				G.				G.		
2	1	2	Sept. 3	5	13	N	Sept. 16	8	8	N	Sept. 21	10	18	P												
29	2	6	Sept. 3	13	17	P	Sept. 20	([b])																		
37	10		Sept. 3	20	13	N	Sept. 16	25	5	N	Sept. 21	[c]10	25	N	Oct. 16	[c]10	34	N	Nov. 19	20	82	P	Feb. 9	25	15 months[d]	
37 A		10	Sept. 3	5	13	P	Sept. 16	10	5	N	Sept. 21	[c]10	25	N	Oct. 16	[c]8	34	N	Nov. 19	[c]10					5½ months	3½ months.
38	7		Sept. 3	30	18	N	Sept. 21	30																	6 months	5¼ months.
43	8		Sept. 3	20	18	N	Sept. 21	30	20	P	([b])															
58	2	5	Sept. 3	15	17	P	Sept. 20	([b])																		
61	2	5	Sept. 3	18	18	N	Sept. 21	[c]10																	6 months	6 months.
65	2	5	Sept. 3	15	18	N	Sept. 21	[c]10	59	N	Nov. 19	15	45	P	Dec. 3	20	68	N	Feb. 9	15					3 months.	21 days.
67	2	9	Sept. 3	24	13	N	Sept. 16	25	5	N	Sept. 21	19	25	N	Oct. 16	15									6 months	5 months.
73	1	4	Sept. 3	8	13	P	Sept. 16	10	5	N	Sept. 21	[c]8	73	N	Dec. 13	15									5½ months	82 days.
75	12		Sept. 3	25	18	N	Sept. 21	35	([e])																	
76	12		Sept. 3	24	([f])																					
78	9		Sept. 3	30	18	N	Sept. 21	[c]10	25	N	Oct. 16	[c]15	34	N	Nov. 19	20									6 months	3½ months.
88	1	7	Sept. 3	13	13	N	Sept. 16	15	5	N	Sept. 21	15	25	N	Oct. 16	15	([g])									
96	1	6	Sept. 3	10	18	N	Sept. 21	12	24	P	Oct. 15	([b])														
49	10		Sept. 16	25	5	N	Sept. 21	[c]10	([h])																	
5	3	6	Sept. 16	10	5	N	Sept. 21	[c]8	([i])																	
74	1	9	Sept. 24	[c]10	([j])																					
69	1	9	Sept. 3	8	18	P	Sept. 21																			

[a] N=negative; P=positive.

[b] Destroyed.

[c] Arsacetin was used instead of arsenophenylglycin.

[d] Died February 11.

[e] Died November 10.

[f] Died September 11.

[g] Died October 22.

[h] Died October 1.

[i] Died September 28.

[j] Died October 3.

THE ETIOLOGY OF BERIBERI.[1]

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The suggestion of a causal relationship between the consumption of white rice and the disease beriberi was first formally made in this country by Braddon (1). The observer also drew attention to the important fact that those who consumed rice which had been parboiled before husking remained free from the disease, as did also the native Malays who consumed rice prepared by primitive methods of pounding and winnowing.

A series of observations made by the writers (2) in 1907 on two parties of laborers, under conditions which excluded or adequately controlled the operation of factors other than diet, confirmed the correctness of this view of the causation of the disease. The prior observations of Fletcher (3) and Lucy (4) in this country and of Dubruel (5) in Indo-China and the recently published observations of Ellis (6) furnish further testimony, and it may now be claimed that the theory rests on a solid basis of evidence.

The mechanism by which white rice was able to produce this result has remained obscure.

Braddon suggested that "the cause of the disorder is not indeed rice, qua rice, or as an article of diet, but diseased rice; rice with which poison derived from decay, due perhaps to some fungus, or mold, or germ, or spore, originally perhaps growing upon the husk, has become mixed during the process of milling; or upon which such fungus may have grown and such poison have been produced after decortication." Eykman (7) from experiments on fowls concluded that a definite poison exists commonly in rice and that for this poison or its effects something in the pericarp is an antidote. Dubruel believed in the ingestion of an organism associated with white rice, which organism multiplying in the body produced the disease.

Following the line of thought suggested by the poison hypothesis, researches were undertaken to determine whether, from white rices actually associated with outbreaks of beriberi, there could be extracted by means of various solvents any substance or substances recognizable by chemical methods as poisonous in character. These researches failed of their object, though it is admitted that the accuracy of the poison hypothesis was not thereby disproved.

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine held at Manila, March 10, 1910.

[2] Director of the Institute for Medical Research; delegate from the Federated Malay States.

[3] Bacteriologist of the Institute for Medical Research.

Certain results which emerged from chemical analysis and histological examination of the rices turned attention to the possibility of an explanation of the course of events on an hypothesis of a defect of nutrition. That this explanation was inadequate, if dietary constituents as estimated by the ordinary analytical methods were alone considered, had been shown in the preliminary investigation.

By a series of experiments on domestic fowls, the details of which will be supplied in a later publication, it was shown that these animals when fed on various kinds of rice were sensitive to differences between them. The fowls were confined in separate compartments and were in all respects under identical conditions. The manner of arrangement of the cages is shown in Plate I, fig. 1.

By further and repeated experiments with rices known to have been associated with outbreaks of beriberi, and with controls under identical conditions fed on parboiled rice, it was established that a certain reaction in fowls might be taken as an indicator of the beriberi-producing power of a given rice when forming the staple of the diet in man. Whether the disease produced in fowls be accepted or not as analogous to beriberi in man, the validity of the arguments here advanced remains unimpaired.

Rices were available that were known to have been associated with outbreaks of beriberi, samples having been taken daily during the continuance of the preliminary inquiry in 1907; also through the courtesy of Dr. J. D. Gimblette and Dr. G. D. Freer we were enabled to procure white rice which was being consumed prior to an outbreak of beriberi among Malays at the Kuala Lumpur police depot, which outbreak ceased on changing the rice supplied to the parboiled variety. It was shown that these rices when fed to fowls constantly produced a certain disease in a large proportion of them, while parboiled rice as constantly failed to produce this result in groups under identical conditions. This disease is characterized by paralysis of the legs (Plate I, fig. 2, and Plate II, fig. 3), followed by paralysis of the wings (Plate II, fig. 4) in the more severe cases. In cases showing a moderate degree of paralysis the gait resembles very closely that seen in beriberi. The nerves of fowls suffering from this disease show typical Wallerian degeneration (Plate III, fig. 5).

It is our belief that this disease, polyneuritis gallinarum, is truly analogous to beriberi in man, similar in its etiology, in its clinical manifestations, and we have shown them to be identical in their pathologic effects, and that its occurrence should be held as important confirmatory testimony of the connection between white rice and beriberi. It is desirable, however, to emphasize the point that the acceptance or nonacceptance of this opinion is immaterial to the argument: for this purpose the occurrence of the disease is employed only as a reaction. The fact that certain white rices when forming the staple of a diet in man produce beriberi rests on quite other testimony than that supplied by experiments on domestic fowls.

The commercial varieties of white rice are numerous, but in this country, apart from the grading as to quality, two are in common use and are known, respectively, as Siam and Rangoon.

From epidemiological considerations and from experimental evidence it appears that Siam rice is considerably more potent in its beriberi-producing powers than Rangoon rice.

The proteins, fats, carbohydrates, and ash were determined for the different varieties of rice which had been employed in the experiments, with the following percentage results calculated on dried material.

	Proteins.	Fats.	Carbohydrates.	Ash.
White rice (Siam)	9.07	0.17	90.11	0.65
White rice (Rangoon)	8.44	0.81	89.90	0.85
Parboiled rice	9.48	0.51	89.12	0.89

A comparison of these results shows that the only marked difference among the rices was in respect to fat, which was most abundant in the variety known as Rangoon, less abundant in parboiled rice, and still less abundant in Siam rice. These observations, taken in conjunction with the experimental results in fowls, excluded the possibility of an explanation of the origin of beriberi on the ground of a deficiency in fat. It will be noted that these analyses did not include an estimation of the relative proportions of the inorganic salts composing the ash, nor did they take account of the manner of combination, organic or inorganic, in which these substances originally existed in the rice grain.

By a method devised in this laboratory, sections of the various rice grains were obtained of sufficient thinness to permit the examination in detail of their histologic characters. By suitable staining methods it was shown that in parboiled rice (Plate III, fig. 7) remnants of the pericarp remained attached to the rice grain, whereas in Siam rice (Plate III, fig. 8) the pericarp and the layers subjacent to it (subpericarpal layers) had been polished away. It would appear that parboiling renders the grain tough and nonfriable, in consequence the subpericarpal layers can not be removed so readily as in the untreated grain. It was further demonstrated that the layers so retained in parboiled rice contained the most of the aleurone and oily material present in rice grains. Rice as prepared by primitive methods (Malay rice) was similarly examined, and, as might have been expected from the pounding to which this rice had been subjected, parts of the subpericarpal layers were chipped off to a varying extent, but on the whole these layers were retained to a greater extent than is the case with white rice.

Early in the course of the experiments the observation was made that parboiled rice subjected to exhaustion with hot alcohol and thereafter carefully dried in the sun to free it from alcohol, produced when fed to fowls a disease indistinguishable from that observed in birds fed on white rice, although such parboiled rice in its original state was incapable of producing this result, however long continued.

The association of the observations referred to in the two preceding paragraphs seemed to point a way to a solution of the problem. It had been shown that white rice as prepared in the mills of this country produced the same results in fowls as white rice known to have been associated with beriberi. If, now, a substance or substances residing in the outer layers which are polished away in white rice and are retained in parboiled rice could be added to white rice and so prevent its harmful effects it was conceived that the nutritive hypothesis would thereby be supported.

In accordance with this idea the following experiments were initiated:

A rice mill in Singapore was visited and there was obtained (A) a quantity of the grain deprived of the husk; (B) a quantity of the polished rice from the same lot of grain, that is, the grain from which the subpericarpal layers had been polished off; (C) a quantity of the polishings, that is, the material removed subsequent to the separation of the husk and which includes the pericarp with the subpericarpal layers. The miller estimates that 40 parts of paddy produce 25 parts of white rice, 5 parts of polishings, and 10 parts of husk. The polishings are sold as food for cattle and the husks are burned as fuel in the mill.

Experiment A.—Twelve fowls were fed on the husked grain for five weeks.

Result: All remained healthy.

Experiment B.—Twelve fowls were fed on the white rice alone.

Result: In five weeks six had developed polyneuritis; two were dead, one having suffered from polyneuritis and one from a disease other than polyneuritis; five fowls remained healthy.

Experiment C.—Twelve fowls were fed on rice taken daily from the same bag as that used in experiment B; in addition, polishings in the form of emulsion, in amount equal to that milled from the quantity of rice consumed, were fed daily by a tube passed into the crop. This quantity was subsequently diminished week by week until only 3 grams of polishings per kilo of body weight were being given daily. This amount sufficed to maintain the fowls in health and in constant weight.

Result: The experiment was continued for seven weeks and all remained healthy.

The result was subsequently confirmed for rice taken from places where known outbreaks of beriberi had occurred.

It will be understood that these three experiments were in progress simultaneously and that the fowls were in all respects under identical conditions.

Experiment D.—Part of the original paddy was taken and milled by a Malay woman by primitive methods into the finished product as eaten by Malays. Eight fowls, fed for five weeks on the rice prepared from the original paddy by the Malay method, remained healthy. Eight fowls only were used for this experiment, as the quantity of paddy then remaining sufficed only for this number for the time it was estimated the experiment would last.

Attention is drawn to the important point that the products used in these experiments were all derived from the same lot of paddy, and the results force us to the conclusion that it is the polishing process, which is essentially at fault: the polishing of white rice removes from the seed some substance or substances essential for the maintenance of the normal metabolism of nerve tissues.

To elucidate the point as to whether rice when freshly milled is less harmful than that which has become stale, an assistant was stationed in Singapore who sent daily to the laboratory by the most expeditious route a quantity of rice milled on the day of dispatch. Twelve fowls were fed on this rice and five developed polyneuritis in four weeks. This result, which is similar to that obtained in other experiments, when fowls were fed on rices milled from four weeks to two years previously, disposes of the suggestion that the harmfulness of white rice is due to its staleness or the development in it of a poisonous substance or substances subsequently to its being milled. The root of the evil lies in the milling process itself. The result further indicates the inadequacy of preventive measures founded on the poison hypothesis in regard to the use of freshly milled rice.

An experiment was now planned to determine whether a parboiled rice proved harmless, could by exhaustion with hot alcohol be reduced to such a condition that it would produce polyneuritis when fed to fowls, and whether the substances so extracted when fed to fowls with a white rice proved harmful could prevent the development of polyneuritis. For this purpose parboiled rice was repeatedly exhausted with hot alcohol. The alcoholic extracts were concentrated *in vacuo* at a temperature of 52°, freed from alcohol and the residue emulsified in distilled water. Experiments with these products showed that fowls fed on the exhausted, parboiled rice contracted polyneuritis, and that birds fed on a white rice proved harmful by previous experiment remained healthy if they received in addition a quantity of the extract.

Having by these and other experiments, the details of which are omitted so as not to encumber the argument, arrived at the point where it was clear that the essential cause of beriberi was to be sought for in a nutritive defect, further efforts were made to determine by chemical methods precise differences between various rices. Such differences, if they are to furnish an adequate explanation for the origin of beriberi, must be in accordance with clinical observations and the experimental results in fowls.

In view of the important rôle played by phosphorus compounds in the metabolism of nerve tissues, the amount of phosphorus in various kinds of rice was determined as phosphorus pentoxide. The result of a large series of observations showed that a reduction in the amount of phosphorus pentoxide obtained from rice was directly related to the probability of the rice producing beriberi; in other words, the higher the phosphorus content of a rice the less was the liability of that rice to produce the disease, and *vice versâ*.

Thus, a sample of parboiled rice which was fed to fowls over many weeks all remaining healthy, was found to contain 0.469 per cent P_2O_5 and a sample of white rice which produced polyneuritis in fowls yielded 0.277 per cent P_2O_5. The rice polishings employed in experiment C yielded 4.2 per cent P_2O_5.

From a series of observations it was determined that a fowl under the conditions of our experiments, weighing from 1,200 to 1,400 grams, required 60 grams of parboiled rice daily to maintain it in health and in nutritive equilibrium. In experiment C it was determined experimentally, the chemical analysis being then unknown, that when fed on white rice a fowl of this weight required the addition of about 3.5 grams of polishings to preserve it in nutritive equilibrium. From the data given above it may readily be calculated what amount of polishings added to white rice, is required to raise the phosphorus content of the white rice diet to that of the parboiled rice. Thus

	Grams P_2O_5.
60 grams of parboiled rice	0.3120
60 grams of white rice	0.1662
Difference	0.1458

Polishings contain 4.2 per cent of phosphorus pentoxide.

Calculated from the phosphorus content, therefore, 3.47 grams of polishings added to the 60 grams of white rice supplied to a fowl of 1,200 to 1,400 grams weight should preserve it in nutritive equilibrium. From experimental observation 3.5 grams of polishings had been shown to accomplish this result. This can scarcely be regarded merely as a coincidence, but its exact significance and importance can not yet be estimated.

Fowls receiving nothing but water do not develop polyneuritis, while fowls receiving only polished rice and water do. No satisfactory explanation of this observation has as yet been obtained, but further researches are in progress. Meanwhile the amount of phosphorus estimated as phosphorus pentoxide contained in a given rice may be used merely as an indicator of its liability or otherwise to produce beriberi.

We are greatly indebted to Mr. B. J. Eaton, chemist in this institute, for valuable assistance in the chemical part of this investigation, and to Dr. R. D. Keith for suggestions as to methods for the examination of the nerves.

SUMMARY.

1. Beriberi is a disorder of metabolism and, as it occurs in this country, is associated with a diet in which white rice is the principal constituent.

2. White rice as produced in the mills here commonly makes default in respect of some substance or substances essential for the maintenance of the normal metabolism of nerve tissues. These substances exist in adequate amount in the original grain and in superabundant amount in the polishings from white rice.

3. The estimation in terms of phosphorus pentoxide of the total phosphorus present in a given rice may be used as an indicator of the beriberi-producing power of such rice when forming the staple of a diet in man.

The prevention of beriberi in this country will be achieved by substituting for the ordinary white rice a rice in which the polishing process has been omitted, or carried out to a minimal extent, or by the addition to a white-rice diet of articles rich in those substances in which such white rice now makes default. One such article which is cheap and readily obtained is the polishings from white rice.

The use of parboiled rice as suggested by Doctor Braddon will achieve a like result, provided that the polishing process is not carried beyond the limited extent now customary.

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ILLUSTRATIONS.

PLATE I.

FIG. 1. Fowl-run, showing arrangement of cages.
2. Fowl fed on white rice. Early stage of polyneuritis.

PLATE II.

FIG. 3. Fowl fed on white rice. Polyneuritis.
4. Fowl fed on white rice. Late stage of polyneuritis.

PLATE III.

FIG. 5. Teased preparation of sciatic nerve of fowl suffering from polyneuritis. Wallerian degeneration.
6. Cross section of rice grain, after removal of the paleæ or husks, showing the pericarp and subpericarpal layers intact.
7. Cross section of rice grain treated by parboiling before milling, showing the subpericarpal layers intact.
8. Cross section of grain of white rice (Siamese). Subpericarpal layers have been removed in polishing.

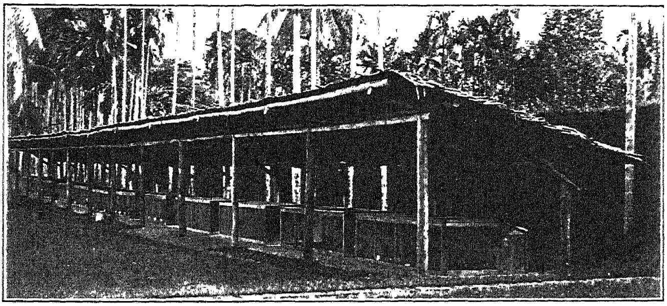

FIG. 1. FOWL RUN, SHOWING ARRANGEMENT OF CAGES.

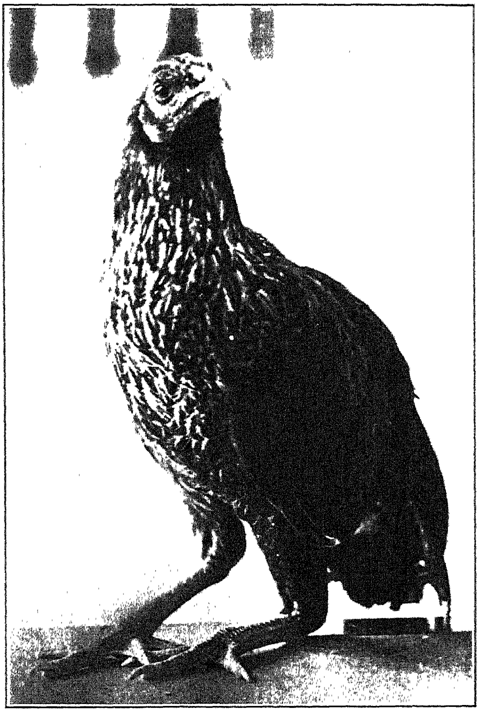

FIG. 2. FOWL FED ON WHITE RICE. EARLY STAGE OF POLYNEURITIS.

PLATE I.

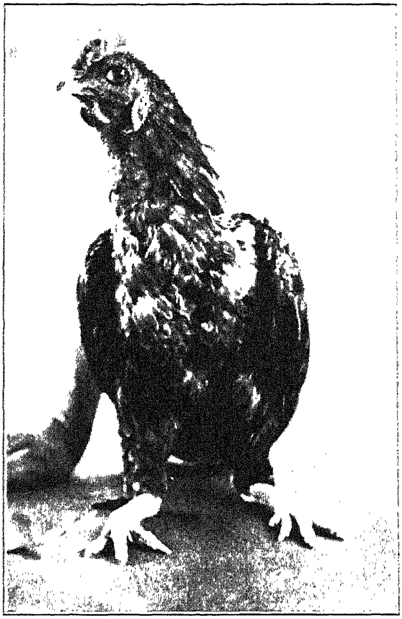

FIG. 3. FOWL FED ON WHITE RICE. POLYNEURITIS.

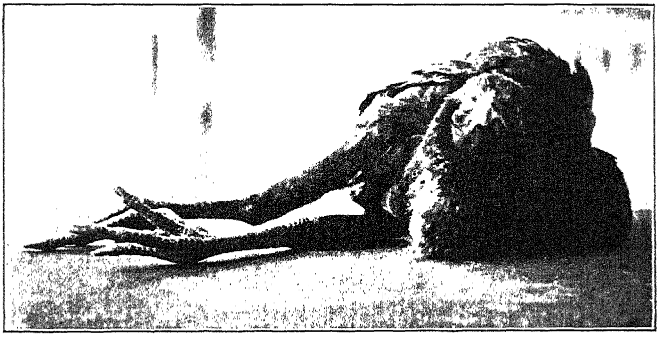

FIG. 4. FOWL FED ON WHITE RICE. LATE STAGE OF POLYNEURITIS.

PLATE II.

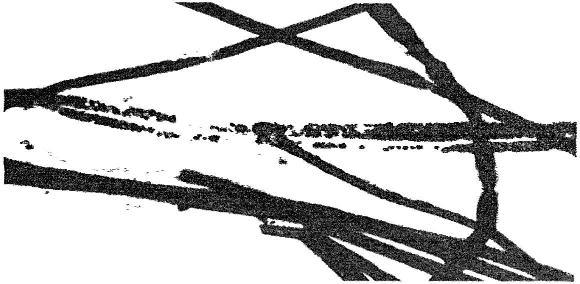

FIG. 5. TEASED PREPARATION OF SCIATIC NERVE OF FOWL SUFFERING FROM POLYNEURITIS. WALLERIAN DEGENERATION.

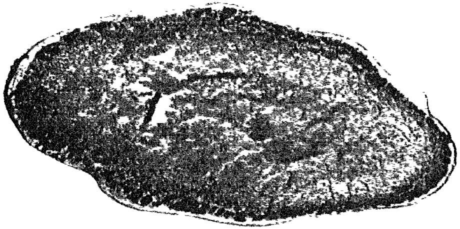

FIG. 6 CROSS SECTION OF RICE GRAIN, AFTER REMOVAL OF THE PALEÆ OR HUSKS, SHOWING THE PERICARP AND SUBPERICARPAL LAYERS INTACT.

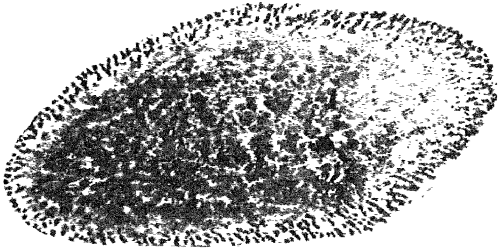

FIG. 7. CROSS SECTION OF RICE GRAIN TREATED BY PARBOILING BEFORE MILLING, SHOWING THE SUBPERICARPAL LAYERS INTACT.

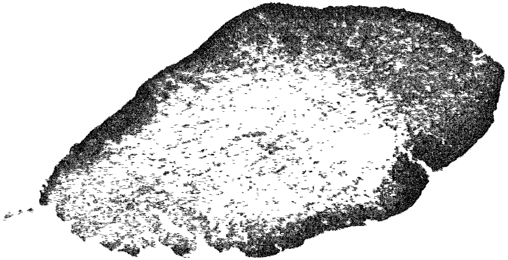

FIG. 8. CROSS SECTION OF GRAIN OF WHITE RICE (SIAMESE). SUBPERICARPAL LAYERS HAVE BEEN REMOVED IN POLISHING.

PLATE III.

ON THE ETIOLOGY OF BERIBERI.[1]

By J. de Haan.[2]

Beriberi has for many years been a subject of study by the government medical laboratory at Weltevreden, and the object of this paper is to communicate the results of all these investigations and to give the point of view which is maintained by us with reference to the etiology, especially for the Tropics, of this interesting disease.

No one hitherto has succeeded in proving beriberi to be caused by a specific microbe, or shown that it should be classed among the infectious diseases. Neither its epidemic nor endemic dissemination, nor the few cases mentioned in literature indicating the possibility of infection from one person to another, should be considered as a proof of its microbic origin, since the clinical symptoms of beriberi—polyneuritis with all its sequels—may be caused by many other factors. My own very numerous attempts to find the *causa morbi* in the blood, the organs, or the excreta of persons suffering from beriberi also have never suceeded, and although I should not wish to consider this as a decisive argument for a nonmicrobic infection, it must be granted that it increases its probability.

By degrees we have gathered a series of facts that may possibly throw some light on this obscure subject.

Doctor Eykman, in the year 1888, observed the appearance among the laboratory fowls of an epidemic of polyneuritis that in many respects resembled beriberi. The clinical symptoms were: Staggering, often followed by total paralysis, paresis of the wings, dyspnœa and cyanosis; followed by death. The post-mortem examination revealed emaciation of the subcutaneous fatty tissue as well as of the muscles, much fluid in the pericardium, degeneration of nerve fibers, but no macroscopic nor microscopic alterations of the brain or of the spinal cord. It was evident that this disease was not caused by an infection with microbes, but that it was closely associated with the food of the fowls. It always appeared after an incubation period of varying duration (ranging from twenty to thirty days, sometimes more) when the birds were fed on boiled rice, the same as was given to the hospital patients. The polyneuritis could not be caused by a poison present in the rice, for fowls sickened much sooner when fed on boiled rice than when the same variety of grain was given unboiled. When they were given unhusked rice, or the so-called red variety, no polyneuritis appeared; the sick ones could even be cured by the latter.

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, at Manila, March 11, 1910.

[2] Director of the Government Medical Laboratory at Weltevreden, Java, Dutch East Indies; delegate from Her Majesty's Government of the Netherlands East Indies.

It then became of great importance to determine the difference between white and red rice. No distinction can be detected between these two varieties when they are unhusked, but it becomes apparent after they have been husked. The grain (endosperm) in the red rice had retained its pericarp (inner skin—Dutch, *zilvervlies*), because there is great coherence between the latter and the endosperm; the pericarp contains a red color in its component cells. Red rice is commonly used as an article of food for animals, and it is eaten by man only in some parts of Java, therefore, no great labor is spent on removing the pericarp. The pericarp must be totally removed to render the grain suitable for the table (cleaned, or white rice), after which manipulation the endosperm alone remains, that is, the grain then consists almost entirely of starch.

These experiments prove that the husks are of no importance in the etiology of polyneuritis. On the other hand, when the diet consists of rice alone, the appearance of the disease depends upon whether the pericarp has been removed or not. Sick fowls recovered when fed on cleaned rice, together with a quantity of the bran from the rice.

Fowls fed on starch (cakes made of sago meal, pearl tapioca, or the starch of the sugar palm tree[3]) also suffered from polyneuritis, but they soon recovered, exactly as fowls did which had fallen ill by being fed on cleaned rice alone, when subsequently given raw meat. The disease also appeared when the birds were fed on sago, tapioca or sugar palm starch, together with a small quantity of meat; on the other hand, those which secured potato-starch, or milk sugar with a small quantity of meat, remained healthy. Polyneuritis never appeared when the fowls were not especially fed. Pigeons contract the disease by being given the same diet as fowls, whereas mammals do not.

From the results of his experiments, Doctor Eykman concludes that polyneuritis is caused by a poison present in starch or developed from it, and that there are one or more constituents in the pericarp of rice which counteract the poison, or prevent its formation. The same conclusions hold with all varieties of rice; neither its origin nor the time during which it has been stored are of the slightest importance.

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[3] *Arenga saccharifera* Labill.

Doctor Eykman's investigations, mentioned above, from 1888 to 1896 caused the sanitary inspector, Doctor Vorderman, to undertake a tour of inspection through all the prisons in Java and Madura to gather exact data on the prevalence of beriberi during the year 1895 and the first half of 1896, and to collect samples of rice in order to discover whether any connection could be established between the prevalence of beriberi in the different prisons and the kind of rice consumed therein.

The result of this inspection was as follows:

> Out of 52 prisons, where cleaned rice constituted the principal article of food, 37 were affected with beriberi, and the average percentage was 71.15. Out of 37 prisons, where rice with the whole of the pericarp constituted the principal article of food, 1 contained beriberi cases, and the average percentage was 2.7. Out of 12 prisons, where half-cleaned rice constituted the chief article of diet, 5 showed beriberi to be present, and the average percentage was 41.46.

The conclusion deduced from these figures, namely, that among men a connection also exists between the prevalence of polyneuritis and rice eating, although criticised by some, must be maintained.

Last year I made a trip to the coal mines of Sawah Loents in Sumatra. Cases of beriberi among the coolies working in the mines at this place are very rare, and I ascertained that the rice eaten by these men was half cleaned.

Statistics on the frequency of beriberi among the Singkehs in the tin mines at Blinjoe in 1908 apparently prove that beriberi was encountered twenty-four times as frequently among the coolies who eat cleaned rice as among those who eat grain which has not lost all of its pericarp.

Doctor Grijns continued these investigations in our laboratory after Doctor Eykman's departure for Holland in 1906. He did not succeed in preventing an outbreak of polyneuritis among fowls fed on cleaned rice by adding to the latter the different salts or the fat, contained in the grain in a smaller quantity than in the pericarp. When the pericarp itself was added in large quantity, then polyneuritis did not appear; but small quantities of the pericarp only delayed its incidence. It was impossible to extract the active constituents from the pericarp.

The beans of *Phaseolus radiatus* Linn., termed *katjang idjo* by the Javanese, not only proved to be capable of preventing an outbreak of the disease among fowls fed on boiled, cleaned rice, but even when it had developed, the birds could very easily be restored to health by eating *katjang idjo*. Another variety, *Cajanus indicus* Spreng. (*katjang iris*), gave the same result. Investigations made in 1909 proved that many other kinds of beans, namely, *katjang bogor* (*Voandzeia subterranea* Thou.), *katjang tjina* (*Arachis hypogæa* Linn.), *katjang pandjang* (*Vigna sinensis* (Linn.) Endl.,) (*V. catjang* (Linn.) Walp.) have the same properties.

Katjang idjo loses its prophylactic and curative power when steamed at 120° for from one to two hours. Fowls even fell ill when fed on steamed beans alone, but it was possible to keep birds which were given steamed *katjang idjo* to which only a small quantity (a few grams) of raw beans had been added, in good health and even sick birds could be cured by the latter mixture. Ducks also contracted polyneuritis when fed on cleaned rice. Fowls also became ill when given unhusked rice, or meat steamed at 120° during two hours. Pigeons fed on meat extracted by boiling, died of polyneuritis.

The disease also appears among fowls fed on raw, unhusked rice, although these instances are very rare. Doctor Eykman, in his later experiments, could not confirm this observation made by Doctor Grijns, but I was able to do so. I kept birds in my own garden, where they were fed only on unhusked and red rice; among these was one cock which suffered repeatedly from the clinical symptoms of polyneuritis and each time was cured by *katjang idjo* and raw meat. The late Mr. de Bruin, of the Veterinary School at Utrecht, observed polyneuritis in a cock fed on a mixture of maize, buckwheat, barley, and husked rice. However, these observations can not be used as an argument against a connection between polyneuritis and rice eating, because polyneuritis may also be produced by many other factors.

Doctor Grijns, in contradistinction to Doctor Eykman, observed that fowls when given milk sugar and potato starch, together with steamed *katjang idjo,* contracted polyneuritis.

Doctor Eykman, after arriving in Holland, repeated the same experiments and, after some failures, produced results identical with those which he had secured in our laboratory. He proved barley, rye, oats, and millet to be excellent food for fowls, but they caused polyneuritis when steamed in an autoclave at 110° to 125°. Sick fowls could be cured by an aqueous extract of rice bran. Potato starch, which he found in his former investigations was incapable of causing polyneuritis, produced the disease when steamed for two hours at 125°. He could not confirm the result obtained by Doctor Grijns in producing polyneuritis by feeding steamed meat.[3] Doctor Eykman, owing to his new experiments, reached the same conclusions as he did from those of 1889 to 1896, namely, that an outbreak of the disease depends upon the presence of definite varieties of starch in the food. He again concluded that the degeneration of the nerve fibers is brought about by a poison which is developed from this starch during digestion. He assumes constituents capable of preventing the formation of this poison to be present in different varieties of food, but believes these to be destroyed by heating to 110° to 125°.

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[3] A. Holst, Experimental studies relating to ship beriberi and scurvy." *Journ. Hyg.* (1907) 7, 619–671, stated that chickens fed on meat steamed at 120° during two hours died from polyneuritis.

Doctor Grijns, after he succeeded in producing polyneuritis in fowls as well as pigeons by feeding them on food without starch, concluded that the nervous system requires definite and until now unknown constituents which are present in different articles of food in widely varying quantities; *katjang idjo* containing a great proportion of the latter, cleaned rice only a few. These constituents can be rendered inactive by steaming at 120° and an article of food which only contains small amounts of them is capable of causing disease of the peripheral nervous system. This author has for a long time been occupied in separating the active constituents from *katjang idjo*, but has not as yet been successful.

Doctor Schaumann, as a result of his investigations on ship beriberi, believed it possible that the nucleins are indispensable to the nervous system. He came to this conclusion because in cases of beriberi the secretion of compounds of phosphoric acid is diminished, and articles of food which are considered as probable factors in the etiology of beriberi, such as, for example, cleaned rice and dried potatoes, contain but a small amount relatively of these compounds, whereas the pericarp of rice and *katjang idjo* have a great quantity. He also proved that a large proportion of the nucleins is decomposed in old beans, which is a reason why articles of food in good condition, by reason of a long voyage or by being stored for a long time, may become unfit to supply the nervous system with sufficient nutriment.

After this communication, Doctor Grijns attempted to cure fowls suffering from polyneuritis by means of nucleins derived from *katjang idjo*, but with negative results. Doctor Schaumann brought forward the same results in his later publications, for in the case of pigeons suffering from polyneuritis, he could produce no effect by giving nucleins prepared from yeast.

In 1909, Doctor Grijns published the following investigation:

> He injected into the peritoneal cavity of healthy fowls the blood of diseased birds (a minimum of 57 cubic centimeters in 12 injections and a maximum of 220 cubic centimeters in 23), but without result. The nerves of diseased fowls, either free or inclosed in collodion sacks and introduced into the peritoneal cavity of healthy birds, did not give rise to polyneuritis. The feeding of healthy fowls on the flesh of diseased birds had no effect, neither did the injection of the blood of the former into the latter accelerate the appearance of polyneuritis in the case of fowls fed on cleaned rice.

In the year 1901 an epidemic of beriberi occurred among the coolies at the coaling station at Sabang (Sumatra). The medical officer there present, Dr. H. L. Roelfsema, could not observe any amelioration in the condition of the patients when he gave them meat and other extra articles of food, but he did observe that the epidemic ended as soon as he prescribed *katjang idjo*. Doctor Hulshoff-Pol repeated these experiments in the lunatic asylum at Buitenzorg. During the period from August 1 to April 30, 1902, the patients from twelve pavilions of the asylum received the following in addition to the ordinary diet:

In 3 pavilions, 150 grams of *katjang idjo;* in 3 pavilions, 300 grams of fresh greens; and in 6 pavilions, ordinary diet. The pavilions were disinfected once a week with carbolic soap, 3 per cent, in order to kill any insects which might be of importance in the dissemination of beriberi.

The following were the results: Seventy lunatics who ate *katjang idjo* did not develop any cases of beriberi. The 86 who were given fresh greens gave 16 cases, and 33 of the 78 who lived in the disinfected pavilions contracted the disease. There were 58 control patients, of whom 19 contracted beriberi.

The curative power of *katjang idjo* was proved by the following:

Out of 64 patients suffering from beriberi, 14 were treated with *katjang idjo,* and these recovered; 20 were left without these beans, and of these 7 died, 6 recovered or improved, and 7 became worse; but after the use of *katjang idjo* the latter also became well.

Doctor Hulshoff-Pol proved that a decoction of *katjang idjo* has the same curative and preventive power as the beans themselves, not only when given to patients suffering from beriberi, but also to fowls with polyneuritis. He prepared the decoction by boiling 1,000 grams of *katjang idjo* with 2.5 liters of water during one and one-half hours, until only 1 liter remained.

In 1908 Dr. Kiewiet de Jonge, in our laboratory, repeated Doctor Hulshoff-Pol's experiments on 384 patients in the lunatic asylum at Buitenzorg. *Katjang idjo* was given to 182 of these, but not to the remaining 202. The result was as follows:

(A) As to the curative action of *katjang idjo:*

Suffered from beriberi and—	With *katjang idjo,* per cent.	Without *katjang idjo,* per cent.
remained unchanged	15.0	23.4
improved	75.0	13.3
became worse	10.0	63.3
died	2.5	30.0

(B) As to the prophylactic action of *katjang idjo:*

Had no beriberi and—	With *katjang idjo,* per cent.	Without *katjang idjo,* per cent.
did not contract the disease	97.2	76.2
contracted it	2.8	23.8
contracted it and died	0	9.3

Thirty-six patients were treated with a decoction of *katjang idjo.* The symptoms of the disease either were greatly ameliorated, or totally disappeared among all of them.

In the year 1909, together with Doctor Grijns, I published a series of experiments describing our attempts to prove the presence of antibodies in the blood serum of beriberi patients, or of fowls suffering from polyneuritis. We did not succeed in proving them to be present. Neither was it possible to find antigen in any of the various organs. We desire to draw attention to this work as giving further confirmation of the identity in the character of the experimental polyneuritis of fowls and polyneuritis epidemica, or beriberi, in man.

The following conclusions are drawn from the above-mentioned investigations.

CONCLUSIONS.

1. The disease described as beriberi, or polyneuritis epidemica, bears a very great resemblance in its etiology, prophylaxis, and therapeutics to the polyneuritis which can be artificially produced in animals, principally in fowls.

2. Just as is the case in the latter, the former is almost always the result of eating cleaned rice, that is, rice deprived of the whole of its pericarp, although other articles of food, prepared in a special manner, may also cause an outbreak of the disease.

3. The pericarp of the rice and also some parts of the grain are removed in the manipulation, by which unhusked rice becomes cleaned rice. Certain constituents of the greatest importance in securing normal nutriment of the peripheral nervous system are lost during this operation.

4. The constituents are neither salts, nor nucleins.

5. Their character is still unknown.

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several of my colleagues who had already been many years in Siam, I was told that beriberi was a rarity. However, on August 29, 1900, our first case was admitted to the Police Hospital in the person of a Siamese constable. Another case came in a month later, but after that no further ones are noted in our Police Hospital register until April, 1901, since which time beriberi has become one of the ordinary diseases seen in that hospital. During this year, 1901, a very severe epidemic broke out amongst the soldiers in the central barracks, several cases were reported from the navy, and cases began to be admitted in increasing numbers to the general hospitals.

Since then, beriberi has taken a prominent place as a cause of invaliding in the public services. In the absence of reliable data for the ordinary civilian population, the following return of cases of and deaths from beriberi recorded in the hospitals, the army, the navy, and the police during eight years may be of interest:

Year (April to March).	Cases.	Deaths.
1901-2	1,128	14
1902-3	1,007	81
1903-4	2,615	161
1904-5	2,813	103
1905-6	3,361	92
1906-7	2,712	101
1907-8	2,427	229
1908-9	4,607	282
Totals	22,670	1,063

It must be noted, however, that these 1,063 deaths give no real conception of the actual death rate, as it was the custom of us all to send our beriberi sick away to their own homes in the country, finding that after a month or two many returned cured. Why such cases should recover much more satisfactorily if sent home is a most important point which will be discussed later. At any rate, here we have a total of nearly 23,000 cases in the public services in eight years. Naturally, the figures for the present year are not yet obtainable, but I have no doubt they will be very high. Compulsory registration of deaths only came into force in Bangkok in October last, but during the three months during which the law has been in force 203 deaths from beriberi have been recorded. So much for the history of beriberi in Bangkok up to a year ago.

Now, as to the cause of beriberi. My experience in Bangkok leads me to confirm absolutely the opinion first expressed by Braddon and lately confirmed by Fraser and Stanton, of Kuala Lumpur, that beriberi is closely associated with the consumption of white, steam-milled rice.

Why this should be so, I am not yet prepared to say. Is it due to the presence of a fungus on the white rice which has become stale, is it the result of want of nitrogen, or is it due to the removal of the oil-containing rind of the grain and so leading to fat starvation? These are points which are still *sub judice* and we await with much interest the elucidation of this fascinating problem. From a practical administrative point of view, at least, we may definitely say that beriberi is apt to attack those who regularly consume white, steam-milled rice, and in support of this view I shall now give you the facts from Bangkok.

1. Beriberi was, so far as we can find out, unknown in Bangkok until white, steam-milled rice began to be retailed locally. It is true that for over ten years before the first outbreak in the jail, white rice was prepared in one or two steam mills in Bangkok, but the whole of this was exported to Europe. One of the first large institutions to be supplied with white, steam-milled rice was the new jail, with the result already recorded. Doctor Hays tells me that it was the prisoners themselves who suggested a return to hand-milled rice, which they had always been accustomed to eat. The change having been made, beriberi died down and has since then given practically no trouble, as the prison authorities have continued to supply this form of rice, which is actually prepared in the jail by convict labor.

During the nineties, attracted by the immense profits which were being made by owners of steam rice mills, many mills were erected, and soon large quantities of white rice were thrown upon the local market. Two factors played into the hands of the rice millers. The first was the abolition of slavery in Siam. Hitherto, the preparation of the household rice was carried on by slave labor, but on the abolition of this practice the price of labor naturally went up. The second factor is a natural corollary of the former, for steam-milled rice could be produced at a much cheaper rate than that manufactured by paid hand labor. By the year 1900 most of the old hand mills had stopped working, and on a diet of steam-milled rice the people began to suffer from beriberi; our first cases being admitted into the hospital during this year.

2. A second fact in support of the white rice theory is the history of our experience in the asylum for the insane. In the year 1900 steam-milled rice was substituted for hand-milled, and beriberi soon appeared. During nine years dieting upon this rice the disease steadily increased in virulence and, in all, 763 patients died of the disease. Early in February, 1908, I determined to try the effects of parboiled rice. Hand mills and all the other apparatus necessary for the purpose were installed in the asylum. We purchased our own paddy, parboiled it, milled it by hand and issued it for the first time on February 15.

Since then not a new case of beriberi has developed amongst those patients who have continued to eat this form of rice, and it is now a year since it was first issued. No other alteration in diet or in hygienic surroundings was made in the asylum.

3. Still another fact in favor of the same theory comes from the Reformatory School at Koh Si Chang in the Gulf of Siam. I can not do better than to quote a note upon this subject forwarded to me by Mr. E. St. J. Lawson, the commissioner of police under whose charge the reformatory is placed. The "station" mentioned is the police station on the island. Mr. Lawson writes:

> The reformatory was started on March 5, 1908. There were no cases of beriberi either amongst the police or in the reformatory until I sent steam-milled rice from Bangkok. I did this because the men complained of the high price of rice on the island and asked me to buy and send to them. In the middle of February, 1909, I started sending hand-ground rice for the station and school use, and changed this to parboiled rice in April. There has not been a single case of beriberi, either in the reformatory or station since the change from steam-milled rice.

To supplement Mr. Lawson's remarks, I may say that there was no medical man on the island, that only serious cases were sent up to Bangkok, that 5 of these, out of a total of 50 boys, were admitted to the hospiatl between November, 1908, and the middle of February, 1909, and that I can not state how many mild cases there may have been.

However, a change of rice from steam-milled to hand-milled and then to parboiled rice, as soon as we could supply it from the asylum, prevented any further cases.

4. The jails in the outlying districts of Bangkok afford us a further proof. In four of these jails, fresh, hand-milled rice is supplied to the prisoners, and in these beriberi is a distinct rarity. However, in two of these jails, steam-milled rice is supplied and beriberi is frequent. Unfortunately, I have not yet obtained details with regard to prisoners either admitted suffering from beriberi, or developing the disease in these jails, or as to the daily average number of prisoners under observation, but the rough figures for the year 1908–9 are as follows: Four jails on hand-milled rice give 5 cases and no deaths; 2 jails on steam-milled rice give 20 cases and 8 deaths.

5. From an administrative point of view, my most striking experience was gained at the Police School in Bangkok. Conscription for the Bangkok police having come into force, some 400 conscripts were admitted to the Police School early in January, 1909. The rice was white, steam-milled, and was supplied by a contractor. It was frequently inspected along with the other articles of food, and on all occasions appeared to be of good quality. However, within a fortnight after commencing to eat this rice, beriberi broke out and at the end of a month 353 out of a total of 400 conscripts had contracted the disease. Practically all these men had come from the country districts outside of Bangkok and most of them had been accustomed to eat only fresh, hand-milled rice.

All the sick men were sent home on a month's leave, at the end of which time very many returned well, many were much improved, while a few were still far from well. On April 31 a second batch of conscripts was admitted, numbering again about 400. By this time, hand mills had been erected at the school and apparatus for the preparation of parboiled rice installed. The healthy were given fresh, hand-milled rice, the sufferers from beriberi parboiled rice. Since then, nearly a year ago, over a thousand men have passed through the school and only a few cases (14 in all) have been detected; and it is more than probable that in the latter instances the men came in already suffering from beriberi. The police prisoners have been fed entirely on parboiled rice and throughout the past year not one case has developed.

6. The last evidence which I shall bring forward in support of the white, steam-milled rice theory is the apparent geographical distribution of the disease in Siam.

In the Province of Bangkok, some 1,700 square miles in extent, we find that beriberi clings to the banks of the Menam River and to the banks of the large, navigable canals which join this river with the adjacent streams throughout the flat, alluvial plains in the neighborhood of the capital. Why is this? Because the river and these canals are the principal means of transport, and along these steam-milled rice from Bangkok is freely hawked. Back from the banks, where communication is difficult, we find that the cultivators mill their own rice and by so doing invariably escape beriberi. Further, amongst a total of 4,550 *gendarmes* scattered throughout the interior of Siam and fed entirely upon hand-milled rice only 6 cases of the disease were reported during the year 1908 to 1909. These 6 cases all occurred in one district, Nakorn Sawan, which stretches on both sides of the River Menam and to which steam-milled rice can gain easy access by boat.

To sum up these facts with regard to etiology: In Siam, as elsewhere in the East, the consumption of white, steam-milled rice would appear to be the principal factor, and the substitution of parboiled rice or of fresh, hand-milled rice is, so far as we know at present, the best practical method of preventing the disease.

Where there is difficulty in getting either of these forms of rice already prepared, see that good paddy is obtained and that it is milled fresh by hand every day. This is especially an important point in connection with coolies engaged on large engineering works, such as railways. In place of transporting white, steam-milled rice to the coolies, see that the food contractors either purchase paddy locally or transport it to the coolie lines, where native hand-mills should be erected and the paddy milled daily by hand. In large cities, where either parboiled rice or hand-milled rice is not obtainable in large quantities, try to induce steam rice-millers to prepare undermilled rice for local consumption.

White rice is the result of "overscouring," as the millers say, but I am told that rice similar to hand-milled can be supplied just as easily, provided there is a demand for it. What is the essential difference between these various forms of rice? They may be divided into two classes, "overmilled" and "undermilled," the distinction being based upon the presence or absence of the pericarp.

White, steam-milled rice is so "overscoured" that none of the pericarp remains. It is overmilled. On the other hand, we find that hand-milled, parboiled, and machine-made "undermilled" rice all retain a considerable proportion of the pericarp, which gives a reddish tinge to these forms of rice in bulk. All three may be classed together as "undermilled."

The whole idea of prevention, then, would seem to be that rice, however milled, which retains a considerable proportion of the pericarp, does not cause beriberi, but that the removal of the outer layers of the grain by reason of the scouring process, either takes away a prophylactic agent, or renders the grain liable to deterioration and the consequent production of some active poison.

POSTSCRIPTUM.

Since writing these notes, prepared in haste on the eve of my departure for Manila, two important events, bearing upon my subject, have occurred. One of these was the receipt, while still in Bangkok, of the latest report by Doctors Fraser and Stanton on "The Etiology of Beriberi." On my voyage here to Manila I have carefully studied this very valuable contribution to the literature on beriberi, and, naturally, it is a matter of considerable satisfaction to me to find that the conclusions of these two able investigators so absolutely corroborate the results of our work in Siam. As they remark, "the root of the evil lies in the milling process itself; the polishing of white rice removes from the seed some substance or substances essential to the maintenance of the normal nutrition of nerve tissues." The deductions of Doctors Fraser and Stanton are the result of carefully conducted scientific experiments, assisted by chemical analyses; my experiments were practical administrative acts, forced upon me by local circumstances, but guided by observation of local conditions. The Siamese in the public services declined to eat parboiled rice owing to its stale, musty flavor. A substitute had to be provided in place of white rice, and this was found in the hand-milled grain.

With regard to parboiled rice, which is now so largely used in public institutions in the Straits Settlements and Federated Malay States, one point is, to my mind, clearly proved by Fraser and Stanton, namely, that its prophylactic powers are not due to any sterilization during the process of parboiling, but to the retention of a considerable proportion of the oil-bearing layers of the seed. This prophylactic property will be found to be distinctly more powerful if the parboiled paddy has been milled by hand.

As I am now treating of the practical prevention of beriberi, and as time does not permit me to deal with any more of the many interesting facts brought forward by Fraser and Stanton, I shall only refer to one more point, namely, the suggestion that rice polishings be added to the diet of those using white rice.

Scientifically, this is a natural deduction from their experiments, but surely Fraser and Stanton must see that their advice is not practical. With people living in close proximity to mills in which white rice is prepared, it might be possible to obtain a supply of these polishings, but even then, in the case of the ordinary native, how can we expect that they will be able to gauge the proportion of the polishings required to make up for the deficiency in the white rice? Further, if the consumer lives in a country where rice is imported, I fear that the supply of these polishings would be a matter of difficulty. I would go even further and say that unless very carefully prepared, rice polishings would not be quite an ideal addition to a dietary, containing as they do much mineral débris from the grinders, dust, filth, etc. No; so far as I can see, the only practical method is to encourage the consumption of undermilled rice. How far legislation might be invoked in this question is too large a subject to be taken up now.

A second important fact learned on my arrival in Manila, is the abandonment by the American Army of the use of imported white rice and the substitution of locally grown and locally milled paddy.

Therefore, it would appear that we all have come to similar conclusions.

In conclusion, I would draw your attention to the name "Siam rice," so often used in writings upon the etiology of beriberi. This is a trade name, and amongst Siam rice we find grain from many of the other neighboring rice-growing countries. It is polished white rice of a certain quality which is inferred by this trade name. Naturally, as delegate from Siam, I am glad not only to have the opportunity of protesting against this use of the term in describing the cause of beriberi, but I believe that I have satisfactorily demonstrated the fact that Siam rice can be shorn of its dangers as a staple article of food through the simple process of "undermilling."

PHOSPHORUS STARVATION WITH SPECIAL REFERENCE TO BERIBERI: I.[1]

By Hans Aron.

(From the Physiological Laboratory, Philippine Medical School.)

It has been argued for a long time that there is a close connection between the food supply and the occurrence of certain diseases appearing in a more or less epidemic form, such as scurvy, beriberi and pellagra. Beriberi, as it appears in the Orient, has been the subject of especially careful studies, and the information which we have received as a result of these investigations allows us to make certain definite statements.

In spite of the claims of various investigators who have described a number of so-called beriberi organisms which all, more or less, have been proved not to be the specific cause of the disease, we can to-day regard it as proved that beriberi is *not an infectious disease.* Of course certain conditions of a general insanitary character, such as living in small, badly ventilated rooms, together with humidity and uncleanliness as well as the influence of tropical climate and other factors of environment, doubtless have some bearing upon the outbreak or occurrence of beriberi. However, the great successes which are recorded in limiting this disease by changes in diet prove beyond any doubt, when taken in connection with careful experimental investigations with different diets on people otherwise living under more or less similar sanitary conditions, that we must regard the diet as the main factor in causing beriberi.

It has been known for a long time in the tropical Orient that people living almost wholly or entirely on rice are more liable to contract the disease than are others. Eykman[2] has already proved that it is not rice in general which must be regarded as the cause of beriberi, but that certain kinds of rice, or, better, rice prepared in a certain way, are most liable to produce the disease. These observations, especially in late years, have been thoroughly confirmed by a number of authors.[3] All observers further agree on this point, that the same kind of rice which causes beriberi, if the diet of the people is based almost entirely on this foodstuff, is eaten without any ill effects if a sufficient amount of other things such as fresh meat, fresh vegetables, and especially certain kinds of beans are taken with it. An ample supply of fresh meat or of the beans, accompanied by a restriction of the quantity of rice consumed, or with a total change of diet, has always proved the best cure for beriberi.[4] The most striking fact in all these observations is the great influence which the preparation of the rice has in its relation to the etiology of beriberi. I will, in order to give a clearer understanding of this phase of the question, give a short description of the preparation of rice for consumption.

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, at Manila, March 11, 1910.

[2] Die Bekämpfung der Beriberi. *Virchow's Arch.* (1897), **149**, 187–194; *Ref. Maly's Jahresb. d. Tierchemie* (1897), **27**, 792.

At first the rice husk must be removed from the grain (in Spanish and native dialect, *palay*). This husk (*ipa*) is never eaten. The grain (*pinaoa*) as it now appears when the husk is broken and thrown away is surrounded by a second, thinner skin of a more or less red or brownish color, which does not render the appearance of the rice very appetizing. This second skin can also be cleaned off by a process of milling between rotating stones which removes it, together with the outside layer of the rice grain; and after this process of milling or polishing, the grain is white and clean and now has the form which the European usually knows as rice. The first rice, which still contains the second skin (the *Silberhäutchen* of the German writers) is that which usually does not cause beriberi; while the grain which is deprived of this skin by the process of polishing must be regarded as quite liable to produce the disease. There are different degrees of polishing, for we find on the market rice which is only slightly polished and grain which has been very highly treated. There are, in addition, certain processes, usually practiced in India and elsewhere ("parboiling") which seem to prevent the thorough removal of the outer parts of the rice, but I am unable to judge of them, since they are not in use in these Islands. The native rice prepared by hand is pounded in a large mortar (Tagalog, *lusong*), and even if milled by a hand mill is never deprived of its outer layers to as great an extent as that milled by large machinery.

Before the exact origin and method of preparing rice capable of causing beriberi was known, it was termed "uncured," while that which did not produce the disease was called "cured" rice. However, while these names are very extensively used, I scarcely think that they convey the right idea.

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[3] *Arch. f. Hyg.* (1906), **58**, 150-170; Fletcher, William. *The Lancet*, London (1907), **1**, 1776; Idem. *Journ. Trop. Med. & Hyg.* (1909), **12**, 127-135; Braddon, W. L. The Cause and Prevention of Beriberi. London. 1907. Idem. *Bombay Med. Congr.* (1909). Fraser, H., and Stanton, A. T. *Bombay Med. Congr.* (1909); An Inquiry Concerning the Etiology of Beriberi. *Studies from the Inst. for Med. Research. Kulua Lampur* (1909).

[4] Waller, F. H. *Geneesk. Tyds. v. Ned. Ind.* (1908), **48**. Hulshoff-Pol, F. *Geneesk. Tyds. v. Ned. Ind.* (1909), **49**. (*Arch. f. Schiffs-u. Trop.-Hyg.* (1909), **13**, 775); Kiewit de Jonge, *ibid.*

I will, therefore, in conformity with Fletcher, designate the first rice as "unpolished" and the second as "polished," or apply the local names, "red" and "white" rice. The unpolished or red rice should be harmless, and we must regard the second process of polishing and milling as that which changes a harmless foodstuff to one harmful under certain circumstances.

This does not mean that the eating of "white" rice under all circumstances causes beriberi. In the first place, it is absolutely necessary that the grain should form the main constituent of the diet, and as the amount of other foodstuffs eaten is smaller in proportion to the quantity of rice consumed, the incidence of the disease under such circumstances is doubtless greater than it would be were a larger amount of other foodstuffs eaten. Furthermore, according to certain authors it seems that white rice stored for a long time, especially in humid rooms and similar places, favors the development of the disease more than the freshly pounded grain, but we must not forget that the latter is almost always prepared by the natives by hand and hence is not so highly polished an article as that kept in storage, which is prepared by machinery.

Eykman,[5] in the course of his investigations on beriberi has shown that chickens fed only on white rice develop a disease which in several respects is similar to beriberi. The most prominent symptoms are a paralysis of the legs and wings and an increasing weakness of the animal, which, if no steps are taken to prevent the further advance of the disease, finally dies. The pathologic examination shows a degeneration of the peripheral nerves, so that the condition has been termed *Polyneuritis gallinarum*. It is very interesting to note from our own standpoint that the same changes in diet, which either avoid or cure beriberi act in an absolutely similar manner upon the fowl.

The disease is only contracted if the fowls are fed on white rice. Those fed on the red grain will suffer very rarely, if at all. An addition of beans or fresh meat to the diet cures the chickens while in the early stages of the disease. Finally, a fowl fed on a sufficiency of beans and white rice or enough meat and white rice will not become ill at all. These experiments have been repeated by Grijns,[6] Maurer,[7] Holst and Fröhlich [8] and also recently by Schaumann,[9] and the observations of Eykman have been fully confirmed. These authors have shown that a similar disease can also be produced in pigeons. In another interesting series of experiments Eykman, Grijns and Axel Holst have further proved that not only white rice, but also certain other foods are liable to produce polyneuritis in chickens and pigeons, and that, especially, long sterilization at a high temperature of certain foodstuffs (such as horse meat) which are absolutely harmless otherwise seems to favor the development of a polyneuritic disease. Holst and Fröhlich[10] were also able to demonstrate that guinea pigs fed on certain one-sided diets, consisting of various kinds of grain, groats, or bread, develop a disease in many respects similar to scurvy.

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[5] *Virchow's Archiv.* (1897), **148**, 523–532; *Arch. Hyg.* **58**, 150–170.

[6] *Geneesk. Tyds. v. Ned. Ind.* (1908), **48**; (1909) **49**.

[7] *Arch. f. Schiffs-u. Trop.-Hyg.* (1909), **13**, 233–252, 284–297.

[8] *Norsk. Magaz. f. Lagevidenskab.* **68**. (*Biochem. Centralb.* (1907), **6**, No. 1225; *ibid*, No. 2478.

[9] *Arch. f. Schiffs-u. Trop.-Hyg. Beiheft* V. (1908), **12**, 37.

DIFFERENCES IN COMPOSITION BETWEEN VARIOUS KINDS OF RICE AND THEIR RELATION TO BERIBERI.

Why does the one variety of rice cause such severe sickness, whereas the other is eaten without any ill effects, and why does the identical, harmful rice not produce the disease if eaten in smaller quantities together with a sufficient amount of certain other foodstuffs?

This question aroused my interest in the study of this disease from the point of view of the physiology of nutrition. We know that fatal diseases can be caused by "spoiled" or bad foods, but these intoxications are brought about by certain *poisonous substances* formed in the food itself. We know further that certain artificially prepared articles of diet are unable to sustain life, but up to the present we have scarcely known any disease which is caused by an apparently normal foodstuff.

Numerous theories to explain the action of different classes of rice exist. In the first instance, a number of authors believe that certain fungi will grow better on the white rice than on the red, because the latter is protected by the pericarp, the introduction of these organisms, fungi, etc., being the real cause of the disease and the rice only an indirect factor. Others, and especially Eykman, regard the white rice as "poisonous," the antidote for all this unknown poison being present in the rice bran as well as in other antiberiberica. Maurer believed beriberi to be produced by the formation of oxalic acid from carbohydrates by a process of fermentation. These hypotheses directly contradict the exact results of experiment.

From a physiologic standpoint, the most probable explanation would be the assumption that by the preparation (milling the rice, sterilizing the food, etc.) certain constituents of importance are taken away, decomposed, or, at least changed so that they now no longer serve their purposes.

Eykman already has considered the subject of the chemical constituents taken away by the process of grinding and which therefore may be lacking in the white rice. If we compare the composition of polished and unpolished rice, we see that the grain by the process of milling becomes poorer especially in ash constituents, fat and cellulose, and also somewhat in protein.

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[10] *Journ. Hyg.* (1907), 7, 619–672.

Balland[11] has shown this very plainly by a number of analyses which are given in the the following table:

Analyses of hand husked, machine husked, ground and polished rice.

Kind of rice.	Water.	Nitrogenous substance.	Fats.	Carbohydrates.	Cellulose.	Ash.
Husked by hand	11.00	9.05	2.80	64.93	1.12	1.10
Husked by machine	13.00	7.82	0.60	77.74	0.28	0.56
Husked and ground	12.90	7.82	0.40	78.20	0.24	0.44
Husked, ground and polished	13.30	7.65	0.30	78.18	0.21	0.36

The main constituents of the ash are the phosphates (53.7 per cent P_2O_5). Therefore Eykman has studied the question as to the extent to which this deprivation of phosphorus may cause the harmful action of white rice, but he could not find sufficient evidence to reach a definite conclusion. Two years ago Schaumann[12] endeavored to show that the disease termed "scurvy of sailing vessels," is caused by a lack of nucleophosphoric acid which is extracted or destroyed by certain sterilization processes, and he argued that a similar lack of organic phosphorus (nucleoproteins) in the food, especially in the white rice, may produce beriberi.

It can easily be believed that a constant lack of phosphorus in the food may bring about a degeneration of exactly those tissues which are rich in phosphorus, namely, of the nerves. I took up the question myself at this point, directing my investigations especially toward the question of the influence of the phosphorus. Meanwhile, there has appeared a second publication by Schaumann,[13] continuing his researches, especially with experiments on animals, and quite recently, in a short paper Fraser[14] and Stanton stated that the phosphorus content of a rice is an indicator of its capability of producing beriberi.

The variations in the content of phosphorus are the most striking changes produced by the process of milling, as the following analyses of different classes of Philippine rice, made by me, will show:

Variety of rice.	P_2O_5.	Protein.
	Per cent.	*Per cent.*
Laguna rice, unpolished	0.557	9.00
Laguna rice, polished	0.314	7.87
"Macan," Bulacan Province, machinery rice	0.340	
"Macan," Bulacan Province, native made, freshly husked rice	0.455	
"Valenciana" rice, highly polished	0.197	
Average Manila rice	0.33	

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[11] *Compt. rend. Acad. sci.* (1895), 121, 561–566.

[12] *Loc. cit. Arch. f. Schiffs-u. Trop.-Hyg. Beiheft.* (1908), 12, 37.

[13] *Arch f. Schiffs-u. Trop.-Hyg. Beiheft.* (1909), 13, 82–90.

[14] The Etiology of Beriberi. *Studies from the Institute for Medical Research, F. M. S. Kulua Lampur* (1910).

I have further obtained a very striking proof of the fact that the rice with a low content of phosphorus will actually cause beriberi, whereas that with a considerably higher content will not, by the study of an outbreak of beriberi on an English steamer which came to this port. Through the courtesy of the captain of this ship I obtained the following data:

> The Indian crew of the steamship *Knight Templar*, used rice almost entirely for food, because the religious laws of this people do not allow them to eat meat except that killed in a special way. For this reason, in addition to rice, only small amounts of mutton could be given to the crew not oftener than once a week. The identical crew had often before sailed on this vessel, and the captain, because of his own previous experience, wished to obtain a certain kind of Indian rice, which he always purchased at Calcutta and which he knew would in all probability not cause beriberi. This I will term "Calcutta" rice. It appears to be a grain which retains a great deal of the pericarp; it therefore is unpolished. The vessel on this particular voyage sailed from Bombay June 5, 1909. Another variety of rice was purchased in Bombay, which I will designate as "Bombay" rice. It was used as food for the crew and they showed no untoward symptoms.
>
> The supply of rice taken from Bombay was exhausted when the vessel reached Liverpool, therefore a fresh supply was purchased. Unpolished rice, in spite of great endeavor, could not be purchased in Liverpool; the grain bought in the latter port ("Liverpool" rice) was of good appearance, white and highly polished. This was given to the crew, beginning about July 25, 1909, under the same conditions and in all likelihood in the same quantity as the "Bombay" rice on the voyage before.

On September 25 a member of the crew became ill and unable to work, but the sickness was not recognized by the captain; but when on October 1 and 2 a man on each day felt weak and could neither walk nor work, the captain then recognized the disease as beriberi. On October 16 the ship arrived at the port of Cavite (in Manila Bay). Here, upon the advice of the boarding officer, the two sick sailors were admitted to the United States Naval Hospital at Cañacao. After October 18 the disease increased so rapidly among the crew that 10 additional men were removed to the hospital on October 25. Here, through the courtesy of Dr. E. R. Stitt, United States Navy, I was able to examine the patients and to confirm the diagnosis of beriberi. One man in the hospital died (probably from paralysis of the diaphragm), but an autopsy was refused by the patient's friends.

The 11 men in the hospital were no longer given rice, but only European food, such as milk, eggs, meat, etc. They showed considerable improvement in a short time. "Bombay" rice and also Philippine red rice was fed to the remaining healthy crew, and only one light case of beriberi developed afterwards. The ship sailed on November 5 with the same crew, the latter having recovered to an astonishing degree in the short time which had elapsed after changing the food.

I have analyzed both varieties of the rice, samples of which I obtained from the captain, and also samples of his former "Calcutta" rice. The differences in the phosphorus content are exceedingly striking; slight variations in the nitrogen content are also to be noted. The following is the table of analyses:

Analyses of "Calcutta," "Bombay," and "Liverpool" rice.

Rice.	P_2O_5.	Protein.	Water.
	Per cent.	*Per cent.*	*Per cent.*
"Calcutta"	0.446	7.75	11.63
"Bombay"	0.408	7.94	11.97
"Liverpool"	0.148	6.69	11.67

Another occasion to study the connection between food and beriberi arose owing to an outbreak of the disease among the lepers at Culion. Here a careful, exact investigation of the data, such as was made in relation to the ship's crew, was impossible, because the people, or at least a part of the people at the leper colony, obtain their own foodstuffs, growing a little rice and catching a few fish, etc., but from the list of foodstuffs which I have given below, it will be seen that in Culion also, rice was the main constituent of the food. Beriberi, to a slight extent, practically was present at all times among the inmates of the colony. In November, 1909, the number of beriberi cases increased rapidly, with a still greater rise in December, 1909, and the first part of January, 1910. The following is the dietary:

Foodstuffs given at Culion per individual per day, in grams.

	August.	September.	October.	November.	December.	January.
Rice, about	700	700	700	700	600	600
Mongo[a]	8	25	36	15	28	90
Meat	40	30	35	40	35	35
Vegetables		26	30	50	35	25
Beans	15	7	7	7	14	8
Tomatoes	16	17	24	16	9	18

[a] A bean grown in the Philippines.

List of special foodstuffs issued on the average per individual per day, in grams.

Dried fish	7 to 8
Tinned salmon	10
Onions	125 to 130
Sugar	5 to 10
Macaroni	1.5 to 2
Chocolate	5
Condensed milk (cubic centimeters.)	5

Incidence of beriberi at Culion in 1909–10.

Month.	Total population.	Deaths.	Deaths from beriberi.	Total number.	In hospital.	
					Admitted sick.	Dismissed cured.
1909.						
January	1,170		6			
February	1,480		13			
March	1,436		15			
April	1,553		15			
May	1,575	47	14			
June	1,719	48	10			
July	1,770	87	8			
August	1,830	61	10			
September	1,776	65	21			
October	1,825	43	4			
November	1,761	80	31	33	1	1
December	1,807	188	68	70	1	1
1910.						
January	1,625	164	103	132	[a]23	6
February 1–8	1,600	26	9	9		

[a] These cases were examined on February 7 and 8, 1910, on an inspection trip to Culion.

The rice was changed in the beginning of January and at the same time the supply of the "mongo"[15] bean was increased.

While a sufficiency of data are not at hand to prove the cause of the outbreak, yet the great reduction in the number of cases after increasing the ratio of *mongo*, which is rich in phosphorus and protein, is striking.

At the suggestion of the writer, Dr. Victor G. Heiser, Director of Health for the Philippine Islands, in February, 1910, gave the order that only unpolished rice (pinaoa) should be supplied to the lepers in Culion. Beriberi disappeared among the lepers in April, 1910, and has not made its reappearance.

THE PHOSPHORUS CONTENT OF POLISHED AND UNPOLISHED RICE IN RELATION TO BERIBERI.

The next question to be considered is: Are these variations in the content of phosphorus as observed in the different kinds of rice sufficient to explain the difference in the action of polished and unpolished rice as foodstuffs capable or not of causing beriberi as well as polyneuritis gallinarum?

[15] *Mongo* is a small bean, *Phaseolus radiatus* Linn. (*P. mungo* Blanco), similar to *katjang idjo*, of Dutch India. The native physicians of this archipelago have proved it to be as valuable as the latter as a popular remedy for beriberi. This bean, according to my analysis, contains the following: Protein, 23.75 per cent; water, 9.56 per cent; P_2O_5, 0.77 per cent; fat, 4.5 per cent; crude fiber, 6.4 per cent.

No further samples of the November and December rice were obtainable, but that used from December 25 until January 12 and after this date has been analyzed and the following per cent of P_2O_5 obtained: rice from December 25 to January 12, 0.321; rice from January 12, 0.463.

From the standpoint of physiological chemistry, the process of milling the rice corresponds to that practised with other cereals and, therefore, the pericarp, removed by the process of milling, corresponds to what we term the bran of wheat or rye. In other words, white rice in composition corresponds somewhat to bread made from fine wheat flour, the red rice to that from whole wheat.

The importance of the bran from wheat and other cereals was formerly not very seriously considered, but more recently Jordan, Hart and Patten,[16] Hart and Andrews,[17] and others, have shown that an organic substance containing phosphorus and termed "phytin," the calcium-magnesium salt of phytic acid, is found therein. Phytic acid, or anhydrooxymethylenediphosphoric acid, was discovered by Posternak[18] as a constituent of green plants, and several investigators have since then demonstrated its wide distribution in the vegetable kingdom. Hart and Andrews[17] found that practically all the phosphorus contained in vegetable foodstuffs is present as salts of phytic acid. This also holds true for rice. Suzuki, Yoshimura and Takaishi[19] proved that 85 per cent of the phosphorus in the bran of the rice is present as phytin. Phosphorus, combined in phytin in contradistinction to that in inorganic compounds, is readily soluble in water or dilute acids and can easily be removed from the bran by processes of washing or extraction. This solubility, as the investigations of Hart and his collaborators[20] have shown, is of great importance in relation to the behavior of phytic acid in metabolism. The phosphorus of phytic acid is readily absorbed, and is therefore a valuable compound in which to supply phosphorus in a form which can readily be assimilated. The effect of so-called organic phosphorus on metabolism in general has already been carefully investigated in the case of lecithin, and the superiority in many respects of organic phosphorus over certain inorganic phosphates seems to be proved.

The investigations, especially of Patten and Hart,[16] Mendel and Underhill,[21] Le Clerk and Cook,[22] proved that the same also holds true for the organic phosphorus compounds which are found in vegetables, namely, phytic acid and its salts. In addition to the readiness with which it is absorbed, phytic acid, according to the experiments of Patten and Hart,[16] is both a diuretic and a laxative, and the well-known laxative action of bran is partly produced by its content of this substance. On the other hand, these authors demonstrated in their work that constipation results if the bran is restricted or if a washed bran, poor in phosphorus, is ingested.

The hypothesis that lack of phosphorus may be an important factor in the etiology of beriberi gains in probability if we consider these facts as they have been found to exist in experiments on cattle, dogs and rabbits, and compare them with what we know concerning the action of different kinds of rice on human beings. For instance, our knowledge that the removal of phytin causes constipation fits well with the general observation that many beriberi patients suffer from extreme constipation.

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[16] *Amer. Journ. Physiol.* (1906), **16**, 268; *Amer. Chem. Journ.* (1904), **37**, 564.

[17] *Bull. New York Agric. Exp. Sta.* (1903), **No. 238.**

[18] *Compt. rend. Soc. biol.* (1906), **55**, 1190.

[19] *Bull. Coll. Agric. Tokyo* (1907), **7**, 495–572.

[20] *Amer. Journ. Physiol.* (1909), **24**, 86–103.

[21] *Amer. Journ. Physiol.* (1906), **17**, 75–88.

[22] *Journ. Biol. Chem.* (1907), **2**, 203.

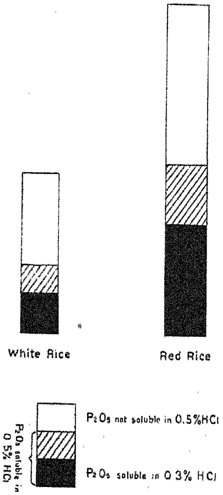
I have made comparative analyses showing the amount of "soluble" phosphorus in polished and unpolished rice and also in rice husk (*darac*) which is left as a result of the polishing process.

THE SOLUBILITY OF P_2O_5 CONTAINED IN WHITE AND RED RICE.

One hundred grams rice were extracted for five hours with 1,000 cubic centimeters 0.5 per cent hydrochloric acid. White rice gave 0.133 gram soluble P_2O_5 or 42.03 per cent of the total P_2O_5. Red rice gave 0.330 gram soluble P_2O_5 or 59.3 per cent of the total P_2O_5.

One hundred grams rice were extracted for two hours with 1,000 cubic centimeters 0.3 per cent hydrohloric acid. White rice gave 0.079 gram soluble P_2O_5 or 25.2 per cent of the total P_2O_5. Red rice gave 0.221 gram soluble P_2O_5 or 39.7 per cent of the total P_2O_5.

The following is a graphic representation of these results and shows them very plainly.



The solubility of the P_2O_5 in rice husk obtained by polishing (darac).

Fifty grams husk, containing 8.27 per cent water, were treated for five hours with 300 cubic centimeters of the solvents given below:

Per cent dissolved by—	P_2O_5.	Nitrogen.
Cold water	0.34	0.269
Hot water	1.70	0.314
0.25 per cent HCl cold	1.66	0.326
0.5 per cent HCl cold	2.04	0.407
1.25 per cent HCl cold	2.25	(0.312)?
Total	4.28	2.00

These analyses strikingly demonstrate not only that the total amount of phosprorus in unpolished rice is considerably higher than in polished, but also that a greater percentage of the total phosphorus in the red variety than in the white is in a readily soluble condition. Therefore, if the same quantity of red as of white rice is eaten, twice the total quantity of phosphorus and nearly three times as much of the soluble phosphorus compounds will be ingested. (See diagram.)

I next endeavored to ascertain if lack of phosphorus, and especially if that in the soluble form, is the cause of the deleterious action of white rice. If this is correct, then the addition of organic phosphorus (phytin) to white rice should render the latter harmless.

I began with experiments on fowls, following the method of Eykman, and convinced myself that chickens fed on white rice contract polyneuritis whereas control birds fed on unhusked and even white rice, if the latter is carefully mixed with rice bran (*darac*), remain healthy for two and a half months.

It is not my intention to prove to what extent the polyneuritis of Eykman and the disease which we term beriberi in man are related, or even to decide whether or not they are one and the same; but I believe these experiments give us a basis of investigation in order to ascertain the importance of the lack of certain food constituents (such as phosphorus) in producing pathologic changes in the nerves and other tissues.

In pursuance of this field of observation, I fed two groups of chickens; the one on white rice and phytic acid prepared from rice husk; the other on white rice alone. The phytic acid was isolated in the following way from the bran of white rice which is separated by the process of polishing between the rotating stones of the mill:

Four kilos of this material (native name *darac*) were placed in a small barrel and extracted with 6 liters of 0.3 per cent hydrochloric acid for from four to six hours, the mixture being stirred from time to time. The extract was filtered, sodium acetate added to the filtrate, and the phytic acid precipitated as its copper salt by means of copper acetate. The phytate of copper was separated, washed with small amounts of water, suspended in this liquid and the copper precipitated by hydrogen sulphide, the precipitate separated by filtration and the filtrate evaporated on a steam bath. A brownish, highly acid sirup was obtained in this way. Its reactions, as well as the manner of its preparation, identified it as phytic acid, according to Patten and Hart.[16]

The free acid was used in the first series of experiments. The rice to be fed was either cooked or only mixed with about 10 cubic centimeters of a solution of phytic acid which corresponded to 0.2 gram of P_2O_5. At first the birds ate this rice very well, but great difficulty in inducing them to take enough of the prepared rice arose subsequently. In a second series of experiments, I therefore endeavored to improve the attractiveness of the preparation of phytin, at first by adding sugar; but as this did not increase its palatability I neutralized the acid by means of sodium or potassium hydroxide. But the alkali salts, while they did not offer as great an obstacle, were also not attractive to the birds. Finally, I prepared calcium phytate by neutralizing a concentrated solution of phytic acid in water by means of a concentrated solution of calcium acetate. The calcium salt of phytic acid is not very soluble in water; it is precipitated and filtered. The preparation has but a slight taste and the odor of acetic acid. In the last two months of the second set of experiments, this preparation was fed directly, each fowl receiving daily in the morning one gram of the calcium phytate.

All the birds which I used were young, still growing, and from about 600 to 1,000 grams in weight. I chose young chickens because I believed that they would contract the disease at an earlier period than old ones. The rice was at first given almost in the dry state, and later, as a change, cooked rice was also prepared, but the birds seemed to take even less of the latter than of the former. A sufficient quantity of the grain was given each day, and care was taken that some rice was always left over. It seems worthy of note that the animals at first instinctively attempted to pick out the grains of rice which were not so highly polished, and if a mixture of white and red rice was given, they would select all the unhusked grains, leaving the others. My general observation is that chickens in the beginning will take white rice in large amounts, but after some time they tire of it and then they do not eat it readily. The course of the experiments is given in the following tables:

EXPERIMENT I.—*Fowls fed on white rice and white rice with phytic acid. Five (six) chickens kept in large wooden cages.*

WHITE RICE.

Mark of fowl.	Month, day, and weight in grams.					Beginning of the disease.	Death.
	Sept. 13.	Sept. 20.	Sept. 27.	Oct. 3.	Oct. 8.		
a	575	464	431	394	351	Oct. 9	Oct. 14
d	469	421	323	319	305	Oct. 8	Oct. 10
e	314	300	233	224	236	Oct. 12	Oct. 15

WHITE RICE AND PHYTIC ACID.

Mark of fowl.	Month, day, and weight in grams.							Result.
	Sept. 13.	Sept. 20.	Sept. 27.	Oct. 3.	Oct. 8.	Oct. 15.	Oct. 21.	
b	500	Escaped Sept. 14.						
c	417	456	439	479	522	505	--------	Transferred to experiment II.
f	340	331	317	288	298	272	253	Oct. 25, died showing symptoms of paralysis beginning Oct. 23.

EXPERIMENT II.[a]—*Fowls fed on white rice, white rice and darac, and white rice and phytic acid.*

Eight (nine) chickens kept in a large yard inclosed by a wire fence.

WHITE RICE.

Mark of fowl.	Beginning of disease.	Death.
g	Nov. 23	Nov. 26
h	Nov. 11	Nov. 13
k	Nov. 9	Nov. 20

WHITE RICE AND DARAC.

Mark of fowl.	Beginning of disease.
l	Healthy until Dec. 31
m	Do.

WHITE RICE AND PHYTIN.[b]

Mark of fowl.	Beginning of disease.	Death.
c (from foregoing experiment)	Healthy until Dec. 31	
e	Dec. 23	Dec. 26
i	Nov. 1	Nov. 18
j	Healthy until Dec. 31	

SUMMARY.—*Duration of life (days).*

Chickens receiving white rice only.		Chickens receiving white rice and phytic acid.	
Mark of fowl.	Days.	Mark of fowl.	Days.
a	33	c	> 120
d	30	f	44
c	34	e	76
g	46	i	38
h	33	j	> 80
k	40		

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[a] This experiment was commenced October 12, 1909, and ended December 31, 1909.

[b] October 13 to October 25, 10 cubic centimeters of phytic acid solution were given daily (0.2 gram P_2O_5); October 26 to October 31, the same solution of phytic acid neutralized by caustic potash; November 1 to December 30, 1 gram calcium phytate; November 7 to November 10, owing to illness of the writer, no phytin was given, but white rice only.

All chickens fed for some four to five weeks on white rice developed the typical symptoms of polyneuritis[23] as they have been described by Eykman and other investigators. These are very characteristic and scarcely need pathologic-anatomic confirmation. The weakness of the legs and the characteristic gait of the birds are sufficient to confirm the diagnosis.

It is evident from these experiments that chickens which are given white rice alone do not live much over thirty-five days, whereas the birds fed on white rice plus phytic acid live for a considerably longer time. One fowl from the first group which received phytic acid, survived for three months, being under observation continually, whereas a second bird fed on white rice together with phytic acid contracted the disease and died, but it did so at a later time than the control chickens fed on white rice only.

In the second set of experiments, I succeeded by the addition of the calcium salt of phytic acid in keeping two chickens alive for nearly three months on white rice only. However, one chicken already became ill after 3 weeks and died on the 38th day. I can not state the exact reason for this result, but I believe it to be true that the bird did not take enough phytin in the beginning of the experiment in which fowls were fed on a mixture of rice and phytic acid and at which period they were more or less able to select those grains of rice which were comparatively not as thoroughly mixed with the preparation.

We may draw the conclusion that without doubt phytic acid renders the effect of a diet of white rice less damaging. I did not have as great success by the use of phytic acid as in feeding red rice, or by adding *darac* (rice husk), neither was the protective effect as great as that described by Eykman when he gave red rice, or added beans or meat to the diet.

Schaumann,[13] in his latest communication, which came into my hands for the first time after I had finished the experiments described above, shows that he was able to protect pigeons from the damaging effect of white rice by the addition of yeast or wheat bran. These experiments increase the number of substances which we already know and which act as a protection against polyneuritis produced by feeding white rice. However, all of these other experiments do not prove *which* constituent of the substances to be added counteract the damaging effect of the white rice. I believe my experiments give sufficient proof *at present* that at least *one of the main factors* in these protective substances must be an organic compound of phosphorus, because of the fact that the addition of such organic phosphorus, as it is present in the rice husk, has a protective action against the damaging effect of the white rice itself. I agree with the interpretation which Schaumann has given to his own experiments and to those of Eykman. He may be correct in considering that the nucleo-protein of yeast is the constituent preventing polyneuritis, but in the case of rice it is my belief that the phosphorus compound which has been designated as "phytin" is the active substance.

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[23] The histologic examination of the *nervi ischiadici* and *tibiales* of these animals and of those described farther on in this paper was kindly undertaken by Dr. Vernon L. Andrews, of the pathological laboratory of the Philippine Medical School. The sections showed plainly a number of degenerated fibers in the nerves.

Although my experiments seem to be sufficiently positive to warrant a continuation along the same line, I have abandoned them at present in order to discover if it is not possible to work with animals other than chickens. These birds are not very appropriate for exact experimentation, and while we can endeavor to produce in them such diseases as polyneuritis, it is very tiresome to carry on close feeding experiments with fowls. I have therefore attempted to feed other animals on white rice or on a food having a similar composition.

Monkeys were fed on white bread made only of wheat flour and water and salt. Such a bread, when fresh, contains about 40 per cent of water, 8 of protein, 52 of carbohydrates, 0.116 of P_2O_5; or, if we reduce the percentages to the same water content as rice, about 10 per cent of protein, 75 of carbohydrate and 0.155 of P_2O_5. Therefore, this bread in its P_2O_5 content corresponds to a very highly polished rice; the protein content is slightly higher, that of carbohydrates somewhat lower, but these differences are really too small to be of any importance.

The animals in the beginning took this bread readily. At first I gave 75 and then 100 grams per monkey of 2,000 grams; this amount being almost entirely eaten up each day, up to the time, when the monkeys became very weak. This amount of bread corresponds to 100 calories per kilo of body weight. It must be remembered that the demand for energy in these animals is very great when we consider their small size, great surface and their excessive muscular activity. The animals (*Macacus philippinensis* Geoff.) were kept in a large, airy yard, covered on top and on one side with wire gauze, thus giving them plenty of air and more space for free movement and gymnastic exercise than is found in the usual cages. Furthermore, the animals were placed at least two in a room so that they would not feel their imprisonment quite so keenly. In working with monkeys this point must not be forgotten.

EXPERIMENT IV.—*Weight of monkeys fed on bread and water.*

Date.	I.	II.	III.	IV.	V.
January 10	1,853	2,083	2,123	----------	--------
January 17	1,324	[a] 1,814	2,131	----------	--------
January 25	1,315	----------	2,087	1,745	1,140
February 1	1,287	----------	2,102	1,722	1,147
February 8	1,077	----------	2,037	1,590	1,130
February 15	1,079	----------	2,005	1,480	1,400
February 23	1,000	----------	1,975	1,545	1,375
February 28	920	----------	1,720	1,530	[b] 1,130
March 1	[c] 842	----------	----------	----------	----------
March 2	----------	----------	[d] 1,745	([e])	----------

[a] Died January 18, strong diarrhœa, unknown origin.
[b] Died February 27, weakness, etc., as described below.
[c] Died March 1, weakness, etc., as described below.
[d] Died March 2, weakness, etc., as described below.
[e] Died March 26, weakness, etc., as described below.

Three animals were selected at first, but one (Number II) died in the beginning of the experiment of a severe diarrhœa of unknown origin. Two others were taken about two weeks later. The experiment demonstrated that bread and water alone are not capable of sustaining monkeys in full health for a longer period than from four to six weeks. In spite of the fact that the animals ate the equivalent of 80 to 100 calories and 0.3 gram protein per kilo of body weight, they died in about six weeks, with signs of general weakness and emaciation. The muscular weakness in some of the monkeys was very prominent. The animals, which in the beginning would run away if approached and if caught would resist their captor with considerable muscular force, were now handled without trouble and were scarcely able to hold themselves with their hands gripping the arm or fingers. Death came at last, the respiration becoming slower and slower, and weaker and weaker. At autopsy no pathologic changes other than those incident upon emaciation and anæmia were noticed. The histologic examination of the nerves has not up to the present been undertaken. No experiments on the action of phytin on monkeys nourished in the manner outlined above were made.

Guinea pigs will not eat white rice, either cooked or uncooked. When given it they die of starvation in from two to three weeks' time.

I attempted, but with considerable difficulty, to feed adult dogs on white rice and lard. A series of experiments on young dogs will be described later, in connection with other work.

Schaumann,[13] in his latest paper, reports that he was able to produce lesions of polyneuritis in dogs, cats, and rats by feeding them horse meat which had been heated in a 20 per cent solution of sodium carbonate for three hours. However, the full details have not as yet been published.

It seems not out of place to mention here some other work which may have an important bearing on the question under consideration.

Quite recently Stepps[24] has shown that mice when fed on a bread made of flour and milk, which had been extracted with ether or acetone and so deprived of the lipoids, died in a few weeks, while they survived if given the unextracted bread or the extracted bread plus the extract. The author emphasizes the absence of fat after this process, but I think that the extraction probably removes the organic compounds of phosphorus (lipoids) and the loss of these bodies makes the bread unfit for food. The action of food poor in phosphorus on young animals has been studied in the last year by Hart, McCollum and Fuller[25] and by Heubner and Lipschütz.[26] In both publications the authors state that pathologic lesions of the skeletal system are the main results of the taking of food lacking in phosphorus, but, in addition, Heubner and Lipschütz report that they have observed nervous symptoms in one of their dogs, and they mention the possible connection of this question with beriberi.

CONCLUSIONS.

If we summarize our experiments and the observations recorded in the literature, we can state as follows:

1. Certain foodstuffs, especially rice, which are relatively poor in phosphorus (phytin) if they are the main or exclusive article of diet for any great length of time, have been shown by various authors to cause beriberi.

2. The process of polishing removes the outer, layers from the rice; these are rich in phosphorus, especially soluble organic compounds of that element (phytin). They are food constituents probably of high physiologic importance.

3. A diet similar to that which is regarded as the probable cause of beriberi if exclusively given for any length of time to animals, is not sufficient to keep them in normal health.

4. Polyneuritis has been observed in chickens receiving a food similar to that which is regarded as causing beriberi, namely, white rice; the addition of organic phosphorus in the form of phytin or its salts considerably, but not entirely, reduces the deleterious effect of a diet (white rice) which can produce polyneuritis in chickens.

[24] *Biochem. Ztschr.* (1909), **22**, 452–460.

[25] *Amer. Journ. Physiol.* (1908), **23**, 246–277.

[26] *Verhandl. 26 Vers. Gesellsch. f. Kinderheilk.* (1909), 149–161.

PHOSPHORUS STARVATION WITH SPECIAL REFERENCE TO BERIBERI: II.

By Hans Aron and Felix Hocson.

In order to reach a definite conclusion concerning the questions under consideration, it is necessary further to prove that phosphorus starvation actually takes place when a man lives on a diet consisting only of polished rice, or on one of similar composition, and that such starvation does not take place if unpolished rice is used to the exclusion of the other variety.

The minimum amount of phosphoric anhydride in the daily food allowance, according to Tigerstedt,[27] Ehrströhm,[28] and Renvall,[29] should be about 3.4 grams of P_2O_5 daily for an average man, namely, 0.06 gram per kilo of body weight.

Now, if we consider the quantity of phosphorus taken in food, the main constituent of which is white rice, this amount will appear to be exceedingly low as compared with that present in a normal European diet.[30]

However, if we take the values given by Ehrströhm and others as normal, then every Filipino living in his accustomed manner should be nearly in a state of phosphorus starvation; for even a diet of fish and rice scarcely furnishes two grams of P_2O_5 daily, which is less than 0.04 gram per kilo of body weight.

Other authors [31] believe the figures given by Tigerstedt and Ehrströhm to be too high and contend that about 0.035 gram P_2O_5 per kilo body weight is sufficient. We quote the following data taken from a publication by Oeri;[32] these show that a quantity less than 1.5 grams of P_2O_5 daily would doubtless be insufficient to fulfill the demands of the body.

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[27] *Handbuch d. Phys. Braunschweig* (1908), 1.

[28] *Skand. Arch. f. Physiol.* (1903), 14, 91.

[29] *Ibid.* (1904), 16, 94–138.

[30] *Deutsches Arch. f. klin. Med.* (1899), 63, 386–422.

[31] Meyer, L. F. *Ztschr. f. phys. Chem.* (1904), 43, 1–10; Magnus-Levy, V. Noorden Handbuch der Pathologie des Stoffwechsels. Berlin, 2d ed. (1906), 1, 457.

Author.	P_2O_5 intake per day.	P_2O_5 in urine.	P_2O_5 in faeces.	P_2O_5 balance.
Sivén	1.023	0.999	0.677	−0.653
	1.464	0.983	0.828	−0.347
	3.545	2.039	1.050	+0.460
Hamalainen and Helme	1.185	0.979	0.559	−0.354
	1.271	0.919	0.463	−0.112
	1.277	0.902	0.585	−0.209
	1.227	0.814	0.534	−0.122

The question as to the minimum amount of phosphorus which is necessary is probably dependent upon conditions very similar to those attending the problem of the minimum amount of protein. The variety and character of the phosphorus compounds taken and certain other conditions inherent in the individuals are probably the determining factors. However, it seemed to be necessary to ascertain if the amount of phosphorus taken by the Filipino in his typical diet is sufficient in quantity, and also how far this amount of phosphorus can be reduced without producing a state of phosphorus starvation; and, further, it seemed necessary to investigate the bearing on metabolism of a diet low in phosphorus, namely, of polished rice, or a similar one richer in this constituent, namely, unpolished rice.

It seemed to us, in undertaking such experiments, very important not only to study the phosphorus, but also the nitrogen metabolism, for the following reasons: A diet known to cause beriberi, consisting almost entirely of rice and deficient in meat, fish, and other substances, is also relatively poor in protein, and it furnishes the latter only in the form derived from plants. Proteins from plants are not as fully digested as those from animals, and, furthermore, as certain quite recent investigations[33] indicate, vegetable protein has not the same value for the body as an equal amount from animals. Finally, metabolism experiments, especially those of Le Clerk and Cook,[34] demonstrate that the addition of organic phosphorus increases the retention of nitrogen, an observation which is in accordance with statements frequently made[35] regarding the close connection between nitrogen and phosphorus metabolism in general.

[32] *Ztschr. f. klin. Med.* (1909), 67, 288–306.

[33] Thomas, Carl. *Arch. f. Anat. u. Physiol.* (1909), 219–302; Michaud, *Ztschr. f. physiol. Chem.* (1909), 59, 405–491.

[34] *Journ. Biol. Chem.* (1907), 2, 203.

[35] Tunnicliffe. *Arch. int. d. Pharm. u. Ther.*, 12, 207.

METABOLISM ON A DIET POOR IN PHOSPHORUS WITH AND WITHOUT THE ADDITION OF THE ORGANIC PHOSPHORUS COMPOUNDS PRESENT IN THE RICE BRAN SEPARATED BY POLISHING.

NORMAL MAN.

Following out the above considerations we first undertook a series of metabolism experiments on normal men, in order to determine the intake and outgo of phosphorus and nitrogen of Filipinos kept on the usual diet, which is low in phosphorus, with and without addition of organic phosphorus in the form of rice bran (rice polish) and of phytin itself. We also, finally, because of the above-mentioned reasons, studied the effects of such a diet, with and without the addition of protein.

For these experiments and for those described later on, we used prisoners in Bilibid Prison, who voluntarily submitted themselves to the changes in diet. We are very much indebted to Doctor Christensen for his kindness in permitting us to use the facilities of Bilibid Hospital and Dr. Pineda for his kind help in the observations. The conditions there existing for carrying on metabolism experiments are very good, and the persons under observation could be kept without any trouble under lock and key, in a quarantine room with cement floor and walls, furnished with only a bed and small table. A chemical balance and the apparatus for collecting urine and fæces were added.

Two normal men were used as subjects for experiment. No. 1 had undergone an operation for hernia three weeks before he subjected himself to the feeding experiments, but had fully recovered. A comparative study was made with a diet not as rich in phosphorus as is usual and with the same diet to which rice bran from polishing had been added. At first we endeavored to feed the man almost entirely on rice, allowing, in the first and second periods, sugar, salt, and coffee as the only additional foodstuffs. However, he rejected his food several times and asked for some fish and other things. Therefore it was necessary to interrupt the experiment at this point and to give a diet of rice, bread, sugar, coffee, and fish. Bread in reality is not a typical constituent of the diet of Filipinos, but we used it because it does not require cooking and therefore simplifies the preparation of the experimental diet. It must also be noted that the bread was white, made of wheat flour and water after the usual manner, and low in phosphorus and protein, but rich in carbohydrates. In this respect it is very similar to highly polished rice.

The rice was of the white variety, but only slightly polished; the fish was one of the larger native species, half-dried and smoked; the bones were carefully removed and the remainder cut into small slices. These pieces were thoroughly mixed, to secure average samples, and 8 portions of 40 grams each were weighed out and kept on ice. A sample was at the same time taken for analysis. Sugar 50 respectively 100 grams, rice 300 (250), bread 300 (250), and coffee 300 cubic centimeters were freshly weighed or measured each day. The rice was all from the same stock and an average sample of it was taken for analysis. Samples of the bread weighing 50 to 100 grams were taken every second day and preserved in formalin. All the samples were finally dried, weighed again, mixed and finely powdered. Coffee secured on several days was mixed and also analyzed. The sugar was fairly pure, and no analyses were necessary. The *darac* or rice husk from the polishing process, which was used in the second period, was heated to 100° for twenty-four hours to destroy organisms which are always present. Four parts, of 75 grams each, were weighed out and a sample was taken at the same time for analysis. In calculating the amount of the *darac* which it was necessary to add, we regarded the bread and rice given in total as "white rice;" and corrected for both, by addition of the bran to "red rice;" 50 grams of bread and 50 grams of rice being replaced by 75 grams *darac*, and, in order to equalize the calories which had been removed from the diet, we increased the sugar ration from 50 to 100 grams. The man received three meals a day: Breakfast at 7 a. m., bread, coffee and sugar; luncheon, 11.30 a. m., rice and fish, with salt *ad libitum;* supper, 5 p. m., bread slightly toasted, coffee, sugar.

The experiment was carried on without difficulty. The unsuccessful days of the first and second period were sufficient to train the man and his attendants carefully to collect the urine and fæces, and to consume completely the food given; so, for example, he removed all remaining particles by licking the plates.

The urine was placed in a pear-shaped receptacle and then poured into a stoppered bottle containing 20 cubic centimeters diluted formalin. In later experiments the urine was preserved with thymol, formalin giving a certain amount of precipitate which made it difficult thoroughly to mix the urine for analysis. Urine was collected every twenty-four hours, from 8 a. m. to 8 a. m., the total quantity was measured and a known fraction was preserved. In subsequent experiments the quantity was measured, and, by the addition of water, it was diluted to an even amount, such as 1,500 or 2,000 cubic centimeters, so as to simplify the preparation of the mixed urine. The fæces were deposited in a large museum jar, closed by a glass cover and containing 100 to 150 cubic centimeters of formalin, a sufficient quantity to deodorize and preserve the excreta. Not infrequently more formalin was added on the second or third day, so as better to penetrate the scybala with the antiseptic. This method, while it does not permit the determination of the total quantity of *fresh* fæces, proved to be very satisfactory under the present conditions, where the laboratory and the experimental subject were so great a distance apart.

The fæces for each period were marked off by carmine, a method which, except in a few instances, gave very satisfactory limitations. An aliquot portion of the urines (one-tenth of the daily amount) from each period was mixed, provided the analysis of an individual urine was not demanded for special reasons.

The total amount of fæces plus water and formalin was determined for each period by weight, and as large a fraction as possible (one-half to two-thirds of the total amount) was dried in a weighed porcelain dish, under addition of sulphuric acid, on a steam bath. The drying process was finished in a steam-heated vacuum-drying apparatus, then the dish with the fæces was exposed to the air for one day, the quantity of air-dried material determined and then finely ground in a mortar, the powder being kept in a closed bottle. Determinations of total nitrogen (Kjeldahl) and phosphorus (Neumann's method) were performed on all samples of foodstuffs, urines and fæces. The somewhat complicated apparatus described by Neumann was not used for the destruction of the organic material, but a simpler device of my own design was employed.[36] The substance to be analyzed was placed in a 750 cubic centimeter Jena round flask with a long neck, 10 to 15 cubic centimeters of sulphuric and nitric acids were added at the beginning, whereas when the digestion approached completion, nitric acid alone was added.

The detailed records of the experiments are given at the end of this paper.

The subject during the first experimental period (III) of four days received 10.99 grams nitrogen and 1.67 grams phosphorus daily; he excreted 10.61 grams nitrogen and 1.66 grams phosphorus per day, so that nitrogen and phosphorus equilibrium practically existed, thus demonstrating that the food as given, representing about 1,900 calories and containing 70 grams of protein per day was sufficient to maintain a man weighing 52.5 kilos and performing practically no work. The intake of phosphorus, 1.67 grams or 0.032 gram of P_2O_5 per kilo of body weight, was absolutely sufficient. This amount is doubtless lower than the figure obtained as a result of experiments on Europeans, which amount has been regarded almost as the minimum amount of phosphorus permissible; but it corresponds approximately to the quantity of phosphorus demanded by dogs per kilo of body weight which, according to the experiments of Meyer,[31] is 0.035 gram only.

During the second period (IV) the man received very nearly the same diet, with the difference that bran from polished rice was added. He took 11.49 grams nitrogen per day, of which 9.61 grams were in the same form, namely, as rice, bread, and fish, as in the foregoing period, whereas 1.88 grams were present in the *darac*. The quantity of nitrogen taken is slightly higher, but it was necessary to assume that the nitrogen compounds in the *darac* are less digestible than those in the other foodstuffs. The quantity of phosphorus (5.46 grams) was more than three times as great as during the first period, but only 1.45 gram of the phosphorus was present in the same foodstuffs as were employed in the first experiment and 4.01 grams were in the *darac* (rice bran).

The outgo of nitrogen was 10.92 grams; that of phosphorus, 4.84 grams; the nitrogen balance was only slightly higher in this experiment than in the first one, but a retention of more than 0.5 gram phosphorus per day took place. The observation is very common that during the taking of a diet rich in phosphorus small amounts of the latter are retained.

The relative distribution of nitrogen and phosphorus in the urine and fæces was as follows: In the first portion of the experiment 24.06

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[36] Handbuch der biochemischen Arbeitsmethoden. Berlin and Wien. (1909), 1, 388.

per cent of the nitrogen and 31.5 per cent of the phosphorus given reappeared in the fæces. A 75 per cent absorption of nitrogen corresponds to the average obtained with a diet more or less of a vegetable character.

McCay,[37] in his metabolism experiments on Bengalis, observed that 23.86 to 25.68 per cent of the nitrogen reappeared in the fæces. His subjects were given a very similar diet, principally vegetable in nature.

In the second part, 32.55 per cent of the nitrogen reappeared in the fæces. If we assume the absorption of nitrogen (and phosphorus) present in the mixed food exclusive of the *darac* to be the same in this part of the experiment as in the preceding, then it follows that 76.7 per cent of the nitrogen in the *darac* was excreted and only 23.3 per cent absorbed. According to this calculation also, the conclusion can be drawn that only 25 per cent of the phosphorus from the *darac* appeared in the urine and 75 per cent in the fæces.

I intentionally do not use the word "absorbed," because we know that the quantity of phosphorus excreted in the fæces is by no means a measure of the amount not absorbed, for a large proportion of the phosphorus is absorbed and *reëxcreted* into the fæces, its distribution between fæces and urine depending much more on other factors than on the absorbability of the phosphorus.

Oeri [32] in a recent set of experiments has shown that the proportion of calcium in the food is a factor determining the distribution of phosphorus in the excreta, urine or fæces. Patten and Hart also, in their experiments on cows fed with wheat bran, have found that the phosphorus of the wheat bran is excreted almost entirely in the fæces, but at the same time they demonstrated that this constituent in the fæces must previously have been absorbed; it is present in the bran as *organic* phosphorus, but is transformed into and excreted as inorganic phosphorus. As this process can not be performed by the digestive enzymes alone, it is more than probable that phosphorus in the form of organic compounds such as phytin is absorbed and reëxcreted into the fæces.

The next step in our investigation was to institute a comparative study of a diet lower than the first both in phosphorus and in nitrogen, and further to study the effect of an addition of organic phosphorus in the form of phytin to it. This portion of the experiment was also conducted as a control to metabolism experiments on a beriberi patient, to be described later. For this reason, as well as to learn the effect of a higher intake of protein, an addition of egg albumen was made in one of the experimental periods (VI). Another prisoner, No. 17794, was selected for the purpose. This man previously had suffered from a slight panaritium on his foot, but had fully recovered at the time the experiment began. He was strong and muscular, and did not spend approximately the entire time lying in bed, as did the first subject, but cleaned his room and did other things. The experiments on this man were divided into three periods, each covering four days. In the first, a diet low in phosphorus was given, in the next, egg albumen, and in the third, phytin was added. This man, weighing 64 kilos, received 400 grams of bread, 300 grams of rice, 75 grams of bacon and 100 grams of sugar daily, thus giving him 41 calories per kilo of body weight. More detailed information concerning the foodstuffs, etc., will be given under the head of the next experiment, which was in part conducted simultaneously with this one. Both men were naturally kept in two different isolation rooms.

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[37] *Sci. Mem. Off. Med. San. Dept. India,* Calcutta (1908), 34, 1-67.

A study of periods V to VII shows that in the first period where the man received bread, rice, bacon and sugar only, and took in daily 9.57 grams of nitrogen and 1.50 grams P_2O_5, the intake of nitrogen as well as that of P_2O_5 *did not cover* the needs of the body. The quantities 0.023 gram P_2O_5 and 0.15 gram nitrogen per kilo of body weight are therefore insufficient. The increase of nitrogen in the diet from 9.58 to 11.06 grams by the addition of egg albumen (period VI) reduced the loss of nitrogen considerably, namely, from 4.67 to 1.98 grams per day.

The loss of P_2O_5 at the same time is slightly decreased, as compared with the foregoing period. While the first man, weighing 52 kilos, with 11 grams nitrogen per day was exactly in nitrogen equilibrium, the other, of 64 kilos weight, with the same intake, lost nearly 2 grams of nitrogen. The absolute requirement of both men would therefore amount to approximately 0.2 gram of nitrogen per kilo of body weight.

Finally, during the last period (VII), with the same intake of nitrogen as in period V, but a large increase in that of P_2O_5, brought about by the addition of 6 grams of phytin daily, 1.5 grams P_2O_5 were retained daily from the amount given; this retention probably being caused by the fact that more than 5 grams of P_2O_5 had been lost from the body during the two foregoing periods (V and VI).

Special attention is called to the nitrogen metabolism. Whereas the intake in period VII is about the same as in period V, the loss of nitrogen from the body is not half so great. This influence of the organic phosphorus upon the nitrogen metabolism is in accordance with the observations of Mendel and Underhill,[21] Le Clerk and Cook,[34] Tunicliff[35] and others, mentioned above. It shows that nitrogen metabolism must not be forgotten while studying that of phosphorus under different conditions of nutrition.

The distribution of nitrogen and P_2O_5 in the urine and fæces during these experiments was as follows: The content of the fæces in nitrogen is nearly the same during the three periods, being about 3.0 to 3.4 grams. This amount would accord with nearly 35 per cent of the intake corresponding to the periods without the addition of protein (V and VII). The values would agree fairly well with those found by other authors for a purely vegetable diet.[38] During period V the output of nitrogen in the urine alone is greater than the amount taken in. In all this series of experiments the quantity of phosphorus which appears in the fæces is somewhat higher than in the foregoing, but this is scarcely regarded as of importance. The fact that in period VII all the phosphorus from the phytin so far as it is again excreted, reappears in the fæces seems to me deserving of more attention, the quantity of phosphorus in the urine not being increased at all. The explanation given above for this excretion of phosphorus through the fæces probably also holds good. (See p. 103.)

Our conclusions, deduced from the above experiments in their relation to beriberi, are as follows:

(1) A diet consisting of bread and rice (both poor in phosphorus), some fat (bacon) and sugar, furnishing 40 calories, 0.15 gram N and 0.025 gram P_2O_5 per kilo body weight does *not* cover the demands of the body for N and P_2O_5 and therefore leads to N and P_2O_5 loss from the body. Addition of protein reduces the N loss of the body and the loss of P_2O_5 slightly.

(2) The addition of phosphorus in the form of phytin prevents a loss of that constituent from the body, and if sufficient of this element is added a storage of phosphorus after a period of phosphorus starvation takes place. The loss of nitrogen from the body is reduced by the addition of phytin, as compared with a corresponding period in which phytin is not given.

(3) A diet consisting of fish, bread, rice, sugar, etc., furnishing 37 calories, 0.2 gram of nitrogen and 0.032 gram of P_2O_5 per kilo of body weight, is sufficient to keep a man in nitrogen and P_2O_5 equilibrium.

(4) The addition of rice bran has a tendency to produce a slight storage of P_2O_5; the rice polish in this respect corresponding to phytin. The phosphorus, both of rice and of phytin, is excreted almost entirely in the fæces.

METABOLISM EXPERIMENTS ON A BERIBERI PATIENT.

We next attempted to study the metabolism of a beriberi patient under the same conditions. The work so far done in this connection is very limited.

Schaumann,[9] in conjunction with his researches, states that the urine in cases of beriberi has a very low content of phosphorus, and Durham[39] found the metabolism in beriberi to be depressed, the urine having a low content of urea, phosphates, etc. I do not believe that these facts are of very great importance, because we know nothing concerning the food taken at the time and its content of phosphorus.

Scheube[40] also has made a number of analyses of urine in cases of beriberi and comes to the conclusion that in this disease metabolism is lowered.

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[38] Yukawa, Geuyo, *Arch. f. Verd.-Krank.* (1909), 15, 477–524, 609–646.

[39] *Brit. Med. Journ.* (1904), 2, 27.

[40] *Deutsches Arch. f. klin. Med.* (1882), 31, 141, 307.

Teruuchi and Saiki,[41] in opposition to Durham, as a result of an experiment on metabolism, state that the destruction of protein is *increased* during beriberi. Finally, Miura,[42] in a recent article on this disease which came to my notice only after this paper had been read before the association, quotes a number of experiments on metabolism which he has made on 4 people suffering from a more or less acute attack of beriberi. It is characteristic that all of his patients were undernourished during this time. The caloric intake per day often was not higher than 250 to 300 calories, on an average not 1,000. The loss in body weight during the short experimental periods was correspondingly high, namely, 55 to 49, 55 to 46, 46 to 42 kilos, etc. He concludes: "In acute, severe beriberi the nitrogen and P_2O_5 excretion is increased in the urine independently of the quantity of urine passed, in subacute beriberi the nitrogen loss is much lower." His results are very much obscured by the fact that his patients were at the same time highly undernourished.

It was our good fortune to encounter one case of typical beriberi in Bilibid Prison which we could use for study of metabolism. The disease is not at all common among the prisoners in this institution; if the diet given to these people and upon which one of us reported [43] during the past year is considered, it is scarcely to be understood how beriberi could be present at all among its inmates. Indeed, every case occurring there would argue against the theory that beriberi is caused by a diet low in phosphorus, unless a reasonable explanation could be produced showing that the man suffering from beriberi had not received the ample and healthful diet of Bilibid Prison. The case which we encountered, prisoner No. 7272, can easily be proved not to have had a full diet just before he contracted the disease.

The records show that this man has been in prison from April 30, 1908, up to the present time, serving a life sentence. Up to September 25, 1909, his conduct was sufficiently good so that he had suffered only light punishment, such as "carrying stone." During this period his full diet was never restricted, but on September 25, 1909, he received his first severe punishment, he being condemned to ten days on *bread and water.*

His second punishment began on October 22, 1909, and from this date up to December 22, 1909, he was placed on bread and water for a total of forty-one days, and on one day he received two meals, consisting only of bread and water.

A summary of these dates and conditions is as follows: From September 25 to December 22 (a total of eighty-eight days), he was on a diet of bread and water during fifty-one and two-thirds days; or, from October 22 to December 22 (a total of sixty-one days), he was on *bread and water* for forty-one and two-thirds days.

On December 22 this prisoner was taken to the hospital with typical symptoms of beriberi. From this time on he was kept in the hospital on a mixed diet and the Filipino assistant, Dr. Pineda, who treated him attempted to induce him to take *mongo;* however, the prisoner had no taste for this food and therefore, when we first saw him, in the beginning of January, he was practically on a diet of rice, together with a certain quantity of fish and meat, milk and bread. The results of the examination are as follows:

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[41] *Mitt. med. Gesellsch.* Tokyo (1905), 19, No. 6.

[42] Beriberi oder Kakke. *Ergeb. d. inn. Med. u. Kinderheilk.* (1910), 4, 280–318.

[43] Aron, *This Journal, Sec. B* (1909), 4, 195.

A Filipino of small stature, 42 kilos in body weight, lying in the bed, unable to raise himself or to stand without assistance. If placed on his feet, he collapses as soon as support is released. Muscles of the leg and arms very weak, knee reflexes absent; dynamometric test of the left hand 30 to 35, right hand 55 to 60. The æsthesiometric test shows that the ability to feel, the sense of touch and reaction to pricking, as well as his ability to distinguish two different spots simultaneously touched, is reduced to a great extent on the legs, to a less degree on the arms and that it is about normal for a Filipino on the forehead. The apex beat in the mammary line, fifth intercostal space, right border of heart on the right line of sternum. Heart sounds normal, pulse 70. The man is somewhat constipated, but digestion and appetite are otherwise apparently normal. *Diagnosis:* beriberi.

On January 6, the man was put in the isolation room which we have described, and kept on a diet of rice, together with a quantity of fish. He was taught to collect his urine and fæces, to consume his food entirely, and the other details of the regimen necessary for experiments on metabolism. The diet to be given in the first set of experiments should be one which would *cause* beriberi; in the next period, organic phosphorus should be added; then a third period, like the first, should follow. In the next period after this, we intended to study the result of an increase of the intake of nitrogen alone without increasing the phosphorus, and in the last we desired to employ a diet more or less like that given to the first man, and which one of us has termed a typical Filipino diet, consisting of rice and fish. It was our further intention to double the two most important periods, namely, those with the diet poor and rich in phosphorus, so as to have a better control. Seven periods were therefore planned, each intended to cover four days, so that twenty-eight days would be necessary for the experiment.

The experiment originally began on January 9, but because of a failure in taking the fæces, we were compelled again to begin on January 10, so that the experiment covered twenty-nine instead of twenty-eight days. The arrangements were in all particulars exactly like those described above. The food used was again analyzed in respect to the rice, bacon, and fish; the bread and coffee were made in the same way as before and the values obtained in the first series were taken. As in the foregoing "normal" periods, we added bacon to the food of this patient so as to make it as deficient in phosphorus as possible. Three samples of bacon were employed: *A* was somewhat lean, containing some muscle fiber, whereas *B* and *C* consisted entirely of fat. The number of calories given, when reduced to the kilo of body weight (44 calories) was at least identical with the calories given to the first prisoners and therefore the food was quite sufficient to sustain a man who was not able to perform any muscular exertion. Phytin was added to the food during the two periods when a diet rich in phosphorus was administerd, so that we might study the result of the ingestion of this organic phosphorus compound in beriberi. The phytin for this purpose was a commercial preparation, kindly delivered to us by the *Gesellschaft für Chemische Industrie*, Basel.

The egg albumen which was given during the period when the protein content of the food was increased was prepared by precipitating the whites of 100 eggs diluted by water, by means of sodium chloride and acetic acid at boiling temperature. The egg albumen was filtered, carefully washed and dried *in vacuo* at 60°. It was then finely powdered and the daily quantity cooked with the rice. Two preparations, termed egg albumen, I and II, showed only a very slight difference in their content of nitrogen. The fish used in the last period was canned salmon, carefully deprived of bones, the quantity needed for the entire experiment being taken at one time, mixed, and then divided into 4 portions of 100 grams each; a fifth portion of 100 grams being put aside and preserved with formalin as a sample for analysis. The samples of fish were kept on ice and, together with the rice, were cooked fresh each day. The rice, up to the last of January, was from the same stock, a white, fairly polished article. This was used up in February and the next supply, which is at present being used, shows a considerably higher content of phosphorus. This change in the supply of rice was disagreeable, but it could not be avoided.

During the first two periods, which we term A and B, the man was on a diet of bread, rice, bacon and sugar, similar to that given to the normal man in period V. He received about 44 calories, 0.18 gram of nitrogen and 0.026 gram P_2O_5 per kilo of body weight.

The result of this diet fully corresponds to that found with the normal man. It is another proof that a diet of bread and rice undoubtedly is not sufficient to fulfill the demand of the body for nitrogen and phosphorus. Therefore, these experiments clearly demonstrate that this same man, during the long time when he was kept on white bread before beriberi appeared, was constantly losing phosphorus and nitrogen.

Phytin was added during periods C and D. Despite the highly increased addition of phosphorus compounds, and in spite of the fact that this man should have a great demand for phosphorus because of his extended phosphorus starvation, he did not, like the normal man, retain phosphorus, but continued to lose this constituent, although in smaller amount than during the foregoing periods (A and B). The nitrogen balance also continued to be negative, almost to the same extent as in the foregoing periods.

Period E followed, in which a diet deficient in phosphorus again was given. During this time the loss in phosphorus in the urine as well as in the fæces was considerably less than during the corresponding periods (A and B), and therefore the relative lowering of the phosphorus balance was somewhat diminished. Possibly the diminution in the loss of phosphorus should be regarded as a result of the treatment with phytin. A marked reduction in the daily quantity of urine also took place, and this fact might also be taken in explanation; but, on the other hand, the reduction in the quantity of coffee may have been of influence.

The amount of nitrogen was increased during the next period (F) by the addition of egg albumen, in quantity so as to contain 8.34 grams instead of about 6.5 grams of nitrogen daily. In the normal man, the loss in nitrogen was reduced correspondingly by this addition, but in the individual suffering from beriberi, the same quantity of nitrogen as before was lost daily. It is still more remarkable that the excess of nitrogen did not appear almost entirely in the urine, but a large proportion was excreted in the fæces. Egg albumen, under normal conditions, should be absorbed almost to the extent of 98 per cent as was the case in period VI, but in this instance at least 25 per cent was lost.

The addition of 100 grams of fish, in period G, finally increased the nitrogen intake to 10.06 grams a day, or 0.25 gram per kilo of body weight. The nitrogen balance now registered only —0.6 gram, which did not represent full nitrogen equilibrium, although the shortage was small.

The phosphorus intake was at the same time increased to 1.91 grams per day, or 0.048 gram P_2O_5 per kilo of body weight. While this amount of P_2O_5 is far below that given during periods C and D, when phytin was added to the diet, the phosphorus balance now showed a daily loss of only 0.13 gram P_2O_5. Therefore, the man was nearly in phosphorus equilibrium. While during this period there was less P_2O_5 taken in, there still was a better retention of this element, probably because of the fact that, during this period, the loss of nitrogen was very small as compared with that in the foregoing periods C and D. It must be assumed that the destruction of the materials of the body containing nitrogen also brings with it the destruction of those containing phosphorus, and that therefore a loss in nitrogen should necessarily also be accompanied by one of phosphorus, regardless of the excess of phosphorus which may be taken in. Of course, as experiment VII has shown, we may find a favorable retention of phosphorus together with a loss of nitrogen, but in this instance the loss in phosphorus had taken place during a short period, whereas in the patient suffering with beriberi the loss of both nitrogen and phosphorus had continued for many weeks.

This view is strengthened by certain differences to be observed between cases of beriberi. A patient just beginning to show symptoms of nervous disorder and of weakness will often recover if his diet is changed in the course of one or two weeks; whereas, on the other hand, in instances where the disease has lasted several months, a long period of treatment is necessary before improvement sets in.

After finishing the metabolism experiment, we kept the patient on practically the same diet as he had received in period G after February 7, and, in addition, he received 4 grams of phytin daily, in two powders. He was maintained in isolation and under close observation. He was able to get up without help on or about February 20, toward the middle of March he could stand with assistance, and also walk a few steps and now he is still weak, but free from clinical symptoms. He certainly has improved to a much greater extent than during the entire month of January, when there was practically no change in his condition. The dynamometric tests give objective data concerning his muscular and general condition.

Dynamometric tests.

Date.	Right.	Left.	Remarks.
January 9	55	35	
January 17	60	35–40	Jan. 18 to 25, 6 grams of phytin daily.
January 25	70	50	
January 30	65	45	
February 7	65	45	From Feb. 7, 4 grams of phytin daily.
February 15	75	50	
March 1	75	50	
March 7	75	55	

The most striking result of these metabolism experiments on a beriberi patient is that at the present stage of the disease he can not utilize the addition of phosphorus in phytin (periods C and D) or of protein (period F) *to the same extent as normal man* (periods IV, VI, and VII), and that he therefore requires a higher intake of nitrogen and phosphorus in similar food to reach nitrogen and phosphorus equilibrium (period G) than does a normal man (period III).

The results of our extended metabolism experiments under varying conditions, without doubt lead to the same conclusions as those of the Japanese investigators, namely, that nitrogen destruction in beriberi is *increased.* The objection that the man may have been undernourished can not be made, as was the case in Miura's experiment, because he took in a higher number of calories than both of the normal men on the same kind of food.

It is not our desire to decide from these experiments alone whether this higher demand is *characteristic* of beriberi or not, nor whether the greater demand for phosphorus and nitrogen is caused by some other reason and therefore predisposes the man to contract the disease, nor whether the higher demand is the result of the long phosphorus and nitrogen starvation which may have weakened the entire system. Further investigations along this line seem to be absolutely necessary.

The last period and the following dietary treatment show that an increased intake of phosphorus and nitrogen have a decidedly favorable influence on the patient. At the same time his nitrogen and phosphorus balance approaches equilibrium, while previously, during the time when there was no improvement, it was negative.

Some points worth mentioning still remain. The excretion of P_2O_5 as well as of nitrogen in period E, after phytin had been given, is considerably smaller than it was previously in periods A and B. The phytin (periods C and D) also increases the amount of total solids in the fæces, having a slight laxative action, without at the same time increasing the loss of nitrogen. The quantity of urine rises in the normal man, not only when phytin but also when *darac* is given; but there seems to have been no effect with the beriberi patient.

We do not believe the question of the effect of a constant phosphorus and nitrogen starvation to be fully solved by a study of the problem of beriberi. If our supposition is correct and if beriberi is caused by a lack of phosphorus and nitrogen in the diet, then there should be a great number of people whose diet is lacking in phosphorus and nitrogen. However, this starvation may not be of sufficient extent as to cause them to be actually ill. These individuals may be somewhat weak, less able to work and easily tired. The scale of transition between strong, healthy men, to those showing the typical paralysis of beriberi is probably extensive. We are fully convinced that the character of the food is not the least important cause of the inability to work which we notice in the lower classes of natives. The great problem of the influence of nourishment upon general health and muscular power is involved in this consideration.

CONCLUSIONS AND SUMMARY.

1. It is highly probable that living for an extended period on a one-sided almost exclusively vegetable diet, which is characterized by its poverty in phosphorus and protein, may result in beriberi.

2. The process of polishing rice removes a fine skin and the outer layers (bran); this rice bran is rich in phosphorus, especially in its organic, soluble form (phytin); the content of phosphorus of the rice is considerably reduced by the removal of the bran.

3. Polished rice, poor in phosphorus, may cause beriberi in man if it is the main constituent of the food; but it is harmless if sufficient other nourishment, rich in phosphorus and protein, is taken. The same polished rice causes a polyneuritis in chickens. White bread, a food of similar chemical composition as regards phosphorus and protein, can not sustain monkeys in normal health if it forms the entire diet.

4. The addition of phytin (the organic phosphorus compound from rice bran) considerably reduces the deleterious effect of white rice on chickens.

5 Metabolism experiments show that a diet such as is described in this paper, which contains about 40 calories per kilo, and which supplies less than 0.2 gram of nitrogen and 0.032 gram of P_2O_5 per kilo of body weight, can not meet the need of a normal man for phosphorus and protein. If phosphorus in the form of phytin or rice bran is added, a part

is stored and a favorable influence on the nitrogen metabolism can also be observed.

6. Metabolism experiments on a beriberi patient in a fairly advanced stage of the disease show that the capability of the man to utilize the nitrogen and phosphorus in the food is reduced; he demands a higher intake of nitrogen and phosphorus than a normal person to attain nitrogen and phosphorus equilibrium. It is especially to be noted that the capability of utilizing additional doses of phytin is considerably less than in that of a normal man under like conditions.

7. While it is certain that phosphorus and nitrogen starvation cause a certain and probably a great number of diseases which we term beriberi, there must be other factors,[44] especially when the œdematous form is observed.

RECOMMENDATIONS.

A very valuable portion of the rice is removed by the process of polishing and a healthy foodstuff transformed into one which is liable to cause a severe disease. Therefore, it should be the endeavor of all physicians to instruct rice producers and rice manufacturers concerning this process, and medical officers who have charge of the purchase of rice in large quantities for native troops, employees, etc., should use only grain which is either not polished or at least but slightly polished.[45]

Where the occurrence of beriberi in certain districts, in institutions, on ships, etc., is possible, care should be taken to give the people forr containing a sufficient quantity of phosphorus and protein. The greatest success would be attained by a large supply of fresh meat, or where this is not available, as in these islands, a sufficiency of the native bean, *mongo.*

A very promising means for the limitation or prevention of beriberi would be the use of the rice bran itself, 50 or 100 grams being cooked with the rice daily, as a protective or as a medicine. This rice bran seems to be the cheapest and most natural supply of the organic phosphorus compound, phytin; the preparation itself, while valuable, being much too expensive to be of any practical use. We are studying the value of rice bran as a protective on the ship *Pathfinder* of the United States Coast and Geodetic Survey, on which outbreaks of beriberi have periodically been recorded. Rice bran as a treatment has proved itself of value at Culion. The combined effect of a slightly increased protein intake with a constant supply of phytin showed favorable results in the treatment of the case in Bilibid, described above.

NOTE.—For the discussion on these papers see the end of this number.

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[44] Nocht. *Arch. f. Schiffs-u. Trop.-Hyg. Beiheft.* (1908), 12, 5.

[45] These recommendations have already been fulfilled for the Philippine Islands by an executive order of His Excellency the Governor-General, by which "the use of polished rice in all public institutions is forbidden."

RECORDS OF THE EXPERIMENTS.

NORMAL MAN 1 (PERIODS III AND IV).

	Date.	Weight	Rice.	Bread.	Sugar.	Fish.	Coffee.	Darac (rice bran).	Car-mine.	Remarks.
		Kilos.	*Grams.*	*Grams.*	*Grams.*	*Grams.*	*Cc.*	*Grams.*		
	Dec. 8	53.4	700	300	50	--------	550	--------	--------	
	Dec. 9	54.3	600	300	50	--------	300	--------	--------	
	Dec. 10	--------	200	300	50	50	300	--------	5 p. m.	
Period III.	Dec. 11	52.5	300A	300	50	[a]40	300	--------	--------	Fæces marked 4 p. m.
	Dec. 12	52.5	300A	300	50	[a]40	300	--------	--------	
	Dec. 13	52.5	300A	300	50	[a]40	300	--------	--------	
	Dec. 14	52.3	300A	300	50	[a]40	300	--------	5 p. m.	
Period IV.	Dec. 15	52.3	250A	250	100	[a]40	300	75	--------	Fæces marked 3 p. m.
	Dec. 16	--------	250A	250	100	[a]40	300	75	--------	
	Dec. 17	--------	250A	250	100	[a]40	300	75	--------	
	Dec. 18	52.5	250A	250	100	[a]40	300	75	5 p. m.	
	Dec. 19	--------	ad libitum.					--------	--------	Fæces marked 9 a. m.

[a] Dried.

Analyses of foodstuffs.

	Nitrogen	P_2O_5.
	Per cent.	*Per cent.*
Fish[a] (dried)	6.30	0.70
Rice A	1.48	0.332
Bread, fresh	1.29	0.116
Coffee, 300 cc.	[b]0.16	[b]0.05

[a] 4.57 per cent fat.

[b] Gram.

Analyses of urines.

Period.	Total quantity.	In 100 cubic centimeters.		Total.	
		Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.
	Cc.	*Grams.*	*Grams.*	*Grams.*	*Grams.*
III	3,992 (3,760)	0.798	0.1141	31.86	4.552
IV	4,545 (4,340)	0.632	0.1213	28.72	5.512

Analyses of fæces.

Period.	Total quantity air dry.	Solids.	Nitrogen.	P_2O_5.	Total quantity.		
					Solids.	Nitrogen.	P_2O_5.
	Grams.	*Per cent.*	*Per cent.*	*Per cent.*	*Grams.*	*Grams.*	*Grams.*
III	163.1	9.09	6.48	1.29	148.3	10.576	2.104
IV	298.0	8.70	5.02	4.51	259.2	14.96	13.84

Absorption.

	Nitrogen.		P_2O_5.	
	Period III.	Period IV.	Period III.	Period IV.
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*
Absorbed	75.94	67.45	68.5	36.6
Excreted in fæces	24.06	32.55	31.5	63.4

PERIOD III.—*December 11 to 14, 1909.*

Food.	Nitrogen.	P_2O_5.	Calories (estimated).
	Grams.	*Grams.*	
200 grams sugar			800
1,200 grams bread	15.48	1.392	2,400
1,200 grams rice	17.76	3.981	4,000
160 grams fish, dried	10.08	1.120	320
1,200 cubic centimeters coffee	0.64	0.200	
Total intake	43.96	6.696	7,520
Per day	10.99	1.674	1,880

	Total.		Per day.			Balance.	
	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.		Nitrogen.	P_2O_5.
	Grams.	*Grams.*	*Grams.*	*Grams.*		*Grams.*	*Grams.*
Outgo, urine	31.860	4.552	7.965	1.138	Intake per day	10.99	1.674
Outgo, fæces	10.576	2.104	2.644	0.526	Outgo per day	10.61	1.664
Total	42.436	6.656	10.609	1.664	Balance	**+0.38**	**+0.010**

PERIOD IV.—*December 15 to 18, 1909.*

Food.	Nitrogen.	P_2O_5.	Calories (estimated).
	Grams.	*Grams.*	
400 grams sugar			1,600
1,000 grams bread	12.9	1.16	2,000
1,000 grams rice	14.8	3.32	3,300
160 grams fish, dried	10.08	1.12	320
1,200 cubic centimeters coffee	0.64	0.20	
300 grams darac	7.52	16.04	250
Total intake	45.94	21.84	7,570
Per day	11.49	5.46	1,890

	Total.		Per day.			Balance.	
	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.		Nitrogen.	P_2O_5.
	Grams.	*Grams.*	*Grams.*	*Grams.*		*Grams.*	*Grams.*
Outgo, urine	28.72	5.512	7.18	1.378	Intake per day	11.49	5.46
Outgo, fæces	14.96	13.840	3.74	3.460	Outgo per day	10.92	4.84
Total	43.68	19.352	10.92	4.838	Balance	**+0.57**	**+0.62**

NORMAL MAN 2 AND BERIBERI PATIENT (PERIODS V TO VIII AND A TO G).

Analyses of foodstuffs.

	Nitrogen.	P_2O_5.
	Per cent.	*Per cent.*
Rice I	1.32	0.28
Rice II	1.19	.57
Bread	1.29	.116
Bacon A	2.90	.215
Bacon B	.32	(.022)
Bacon C	.41	(.028)
Salmon	3.78	.42
Egg albumen I	13.71	----------
Egg albumen II	13.58	----------
Phytin	----------	44.24
Capsules[a]	14.66	----------
Coffee, 500 cubic centimeters	[b].026	[b].016

[a] 10 capsules = 2.47 grams.
[b] Gram.

Normal Man 2.

Period and date.		Exper. Day.	Weight.	Rice.	Bread.	Sugar.	Coffee.	Bacon.	Egg albumin.	Capsules.		Urine.		Fæces.
										Phytin.	Carmine.	Total quantity.	Diluted to	
			K.	*G.*	*G.*	*G.*	*cc.*	*G.*	*G.*			*cc.*	*cc.*	
	Jan. 25	1	64.3	ad libitum.					------	--------	5 p. m.	------	------	
V	Jan. 26	2	64.3	300 I	400	100	200	75 C	------	--------	----------	1,370	1,500	Marked off 10 a. m.
	Jan. 27	3	63.9	300 I	400	100	200	75 C	------	--------	----------	[a]740	1,000	
	Jan. 28	4	63.9	300 I	400	100	200	75 C	------	--------	----------	1,330	1,500	
	Jan. 29	5	63.7	300 I	400	100	200	75 C	------	--------	4.30 p. m. 4 caps.	1,750	2,000	
VI	Jan. 30	6	64.1	300 I	400	90	300	75 C	12 I	--------	----------	1,490	1,500	Marked off 10 a. m.
	Jan. 31	7	63.7	300 I	400	90	300	75 C	12 I	--------	----------	2,310	2,500	
	Feb. 1	8	63.7	300 II	400	90	300	75 C	12 II	--------	----------	1,495	1,500	
	Feb. 2	9	64.1	300 II	400	90	300	75 C	12 II	--------	5 p. m. 4 caps.	1,200	1,500	
VII	Feb. 3	10	64.3	300 II	400	100	300	75 C	------	5 caps. 6 g.	----------	2,200	2,500	Marked off 11 a. m.
	Feb. 4	11	-----	300 II	400	100	300	75 C	------	5 caps. 6 g.	----------	2,370	2,500	
	Feb. 5	12	63.9	300 II	400	100	500	75 B	------	5 caps. 6 g.	----------	1,960	2,000	
	Feb. 6	13	63.9	300 II	400	100	500	75 B	------	6 caps. 6 g.	4.30 p. m. 3 caps.	2,220	2,500	
	Feb. 7	14	-----	ad libitum.					------	--------	----------	------	------	Marked off 8 p. m.

[a] Dark.

Analyses of urines, V to VII.

Period.	Total quantity.	In 100 cubic centimeters.		Total.	
		Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.
	cc.	*Grams.*	*Grams.*	*Grams.*	*Grams.*
V	6,000 (5,190)	0.723	0.1157	43.38	6.94
VI	7,000 (6,495)	0.552	0.08956	38.64	6.269
VII	9,500 (8,750)	0.3476	0.06576	33.02	6.250

Analyses of fæces, V to VII.

Period.	Total quantity air dry.	Solids.	Nitrogen.	P_2O_5.	Total quantity.		
					Solids.	Nitrogen.	P_2O_5.
	Grams.	*Per cent.*	*Per cent.*	*Per cent.*	*Grams.*	*Grams.*	*Grams.*
V	209	89.42	6.49	1.40	186.9	13.56	2.93
VI	202	78.60	6.70	1.21	158.8	13.50	2.44
VII	192.3	89.42	6.73	3.84	172.0	12.94	7.38

Period V.—*January 26 to 29, 1910.*

Food.	Nitrogen.	P_2O_5.	Calories (estimated).
	Grams.	*Grams.*	
1,200 grams rice	15.84	3.92	4,000
1,600 grams bread	20.64	1.86	3,200
300 grams bacon C	1.23	0.08	1,600
800 cubic centimeters coffee	0.44	0.13	
400 grams sugar			1,600
4 capsules	0.14		
Total intake	38.29	5.99	10,400
Per day	9.57	1.50	2,600

	Total.		Per day.			Balance.	
	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.		Nitrogen.	P_2O_5.
	Grams.	*Grams.*	*Grams.*	*Grams.*		*Grams.*	*Grams.*
Outgo, urine	43.38	6.94	10.85	1.74	Intake per day	9.57	1.50
Outgo, fæces	13.56	2.93	3.39	0.73	Outgo per day	14.24	2.47
Total	56.94	9.87	14.24	2.47	Balance	-4.67	-0.97

PERIOD VI.—*January 30 to 31, February 1 to 2, 1910.*

Food.	Nitrogen.	P_2O_5.	Calories (estimated).
	Grams.	*Grams.*	
600 grams rice I	7.92	1.95	4,000
600 grams rice II	7.14	3.42	
1,600 grams bread	20.64	1.86	3,200
300 grams bacon C	1.23	0.08	1,600
24 grams egg albumen I	3.28		180
24 grams egg albumen II	3.26		
1,200 cubic centimeters coffee	0.62	0.20	
360 cubic centimeters sugar			1,440
4 capsules	0.15		
Total intake	44.24	7.51	10,420
Per day	11.06	1.88	2,605

	Total.		Per day.			Balance.	
	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.		Nitrogen.	P_2O_5.
	Grams.	*Grams.*	*Grams.*	*Grams.*		*Grams.*	*Grams.*
Outgo, urine	38.64	6.27	9.66	1.57	Intake per day	11.06	1.88
Outgo, fæces	13.50	2.44	3.38	0.61	Outgo per day	13.04	2.18
Total	52.14	8.71	13.04	2.18	Balance	**−1.98**	**−0.30**

PERIOD VII.—*February 3 to 6, 1910.*

Food.	Nitrogen.	P_2O_5.	Calories (estimated).
	Grams.	*Grams.*	
1,200 grams rice II	14.28	6.84	4,000
1,600 grams bread	20.64	1.86	3,200
150 grams bacon B	0.38	0.03	
150 grams bacon C	0.62	0.04	1,600
1,600 cubic centimeters coffee	0.83	0.26	
400 grams sugar			1,600
24 grams phytin		10.62	
24 capsules	0.90		
Total intake	37.65	19.65	10,400
Per day	9.41	4.91	2,600

	Total.		Per day.			Balance.	
	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.		Nitrogen.	P_2O_5.
	Grams.	*Grams.*	*Grams.*	*Grams.*		*Grams.*	*Grams.*
Outgo, urine	33.02	6.25	8.26	1.56	Intake per day	9.41	4.91
Outgo, fæces	12.94	7.38	3.23	1.85	Outgo per day	11.49	3.41
Total	45.96	13.63	11.49	3.41	Balance	**−2.08**	**+1.50**

Beriberi patient.

Period and date.	Exper. Day.	Weight.	Rice.	Bread.	Sugar.	Coffee.	Bacon.	Capsules.		Urine.		Faeces.
								Phytin.	Carmine.	Total quantity.	Diluted to—	
		K.	*G.*	*G.*	*G.*	*cc.*	*G.*			*cc.*	*cc.*	
Jan. 9	1	40.8	200 I	300	100	500	30 A	--------	5 p. m. 4 caps.	800	1,000	
A Jan. 10	2	40.8	200 I	300	100	500	30 A	--------	----------	740	1,000	Marked off 8 a. m.
Jan. 11	3	40.8	200 I	300	100	500	30 A	--------	----------	1,490	1,500	
Jan. 12	4	40.8	200 I	300	100	500	30 A	--------	----------	2,940	3,000	
Jan. 13	5	40.8	200 I	300	100	500	30 A	--------	----------	2,720	3,000	
B Jan. 14	6	40.8	200 I	300	100	500	30 B	--------	----------	2,360	2,500	1 p. m. by regular course.
Jan. 15	7	40.6	200 I	300	100	500	30 B	--------	----------	1,100	1,500	
Jan. 16	8	40.8	200 I	300	100	500	30 B	--------	5 p. m. 4 caps.	1,230 1,690	1,500 2,000	
Jan. 17	9	40.4	200 I	300	100	500	30 B	--------	----------	2,440	2,500	
C Jan. 18	10	40.4	200 I	300	100	500	30 B	5 caps. 6 g.	---------	2,075	2,500	3.30 p. m. marked off, not sharp.
Jan. 19	11	40.4	200 I	300	100	500	30 B	5 caps. 6 g.	---------	2,900	3,000	
Jan. 20	12	40.2	200 I	300	100	500	30 B	5 caps. 6 g.	---------	2,375	2,500	
Jan. 21	13	40.4	200 I	300	100	500	30 B	5 caps. 6 g.	---------	2,300	2,500	
D Jan. 22	14	40.4	200 I	300	100	500	30 B	5 caps. 6 g.	---------	3,000	3,000	4 p. m. by regular course.
Jan. 23	15	40.2	200 I	300	100	500	30 B	5 caps. 6 g.	---------	1,900	2,000	
Jan. 24	16	40.2	200 I	150	100	----	30 B	5 caps. 6 g.	---------	1,400	1,500	
Jan. 25	17	40.0	200 I	300	100	500	30 B	5 caps. 6 g.	4.30 p. m.	1,730	2,000	
E Jan. 26	18	40.0	200 I	300	100	500	50 C	--------	----------	2,865	3,000	4 p. m. marked, not sharp.
Jan. 27	19	39.8	200 I	300	100	300	50 C	--------	----------	2,350	2,500	
Jan. 28	20	39.6	200 I	300	100	200	50 C	--------	----------	[a]500	1,000	
Jan. 29	21	40.0	200 I	300	100	----	50 C	--------	5 p. m. 4 caps	[a]445	1,000	
F Jan. 30	22	41.2	200 I	300	90	300	50 C	[b]12 g.	----------	1,170	1,500	10 a. m. marked off.
Jan. 31	23	41.2	200 I	300	90	300	50 C	[b]12 g.	----------	1,785	2,000	
Feb. 1	24	40.8	200 II	300	90	----	50 C	[b]12 g.	----------	1,205	1,500	
Feb. 2	25	40.8	200 II	300	90	----	50 C	[c]12 g.	5 p. m. 4 caps.	960	1,000	
G Feb. 3	26	40.8	200 II	300	100	----	------	[d]100 g.	----------	1,575	2,000	7 p. m. marked off.
Feb. 4	27	-----	200 II	300	100	----	------	[d]100 g.	----------	1,230	1,500	
Feb. 5	28	41.0	200 II	300	100	----	------	[d]109 g.	----------	2,840	3,000	
Feb. 6	29	40.6	200 II	300	100	----	------	[d]100 g.	4.30 p.m. 3 caps.	995	1,000	
Feb. 7	30	-----	ad libitum.					--------	----------	-------	------	11 a. m. marked off.

[a] Very dark. [b] Egg albumen I. [c] Egg albumen II. [d] Fish.

Analyses of urines, A to G.

Period.	Total quantity.	In 100 cubic centimeters.		Total.	
		Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.
	cc.	*Grams.*	*Grams.*	*Grams.*	*Grams.*
A	8,500 (7,890)	0.2872	0.0730	26.41	6.21
B	10,000 (8,820)	0.2154	0.0496	21.54	4.96
C	10,500 (9,650)	0.2094	0.050	21.99	5.25
D	8,500 (8,030)	0.272	0.05144	22.12	4.37
E {2 days	5,500 (5,215)	0.1995	0.03740	10.97	2.87
E {2 days	2,000 (945)	0.035		6.60	
F	6,000 (5,120)	0.3986	0.05604	23.92	3.36
G	7,500 (6,640)	0.3884	0.06036	29.13	4.53

Analyses of fæces, A to G.

Period.	Total quantity air dry.	Solids.	Nitrogen.	P_2O_5.	Total quantity.		
					Solids.	Nitrogen.	P_2O_5.
	Grams.	*Per cent.*	*Per cent.*	*Per cent.*	*Grams.*	*Grams.*	*Grams.*
A	164.0	94.54	8.12	1.78	155.1	13.32	2.92
B	174.5	96.44	7.90	1.93	168.3	13.79	3.37
C	200.0	96.24	6.77	5.77	192.5	13.54	11.54
D	234.7	89.15	6.39	5.27	208.6	15.00	12.36
E	195.6	91.48	7.58	1.34	178.9	14.83	2.62
F	189.7	86.63	9.38	1.67	164.3	17.79	3.16
G	156.0	93.92	8.60	2.34	146.5	13.42	3.65

PERIOD A.—*January 10 to 13, 1910.*

Food.	Nitrogen.	P_2O_5.	Calories (estimated).
	Grams.	*Grams.*	
800 grams rice I	10.56	2.44	2,650
1,200 grams bread	15.48	1.39	2,400
120 grams bacon A	3.48	0.26	600
2,000 cubic centimeters coffee	1.04	0.32	
400 grams sugar			1,600
Total intake	30.56	4.41	7,250
Per day	7.64	1.10	1,810

	Total.		Per day.			Balance.	
	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.		Nitrogen.	P_2O_5.
	Grams.	*Grams.*	*Grams.*	*Grams.*		*Grams.*	*Grams.*
Outgo, urine	26.41	6.21	6.60	1.55	Intake per day	7.64	1.10
Outgo, fæces	13.32	2.92	3.33	0.73	Outgo per day	9.93	2.28
Total	39.73	9.13	9.93	2.28	Balance	−2.29	−1.18

PERIOD B.—*January 14 to 17, 1910.*

Food.	Nitrogen.	P_2O_5.	Calories (estimated.)
	Grams.	*Grams.*	
800 grams rice I	10.56	2.44	2,650
1,200 grams bread	15.48	1.39	2,400
120 grams bacon B	0.38	0.03	600
2,000 cubic centimeters coffee	1.04	0.32	
400 grams sugar			1,600
4 capsules	0.15		
Total intake	27.61	4.18	7,250
Per day	6.90	1.05	1,810

	Total.		Per day.	
	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.
	Grams.	*Grams.*	*Grams.*	*Grams.*
Outgo, urine	21.54	4.96	5.39	1.24
Outgo, fæces	13.79	3.37	3.45	0.84
Total	35.33	8.33	8.84	2.08

	Balance.	
	Nitrogen.	P_2O_5.
	Grams.	*Grams.*
Intake per day	9.90	1.05
Outgo per day	8.84	2.08
Balance	**−1.94**	**−1.03**

PERIOD C.—*January 18 to 21, 1910.*

Food.	Nitrogen.	P_2O_5.	Calories (estimated).
	Grams.	*Grams.*	
800 grams rice I	10.56	2.44	2,650
1,200 grams bread	15.48	1.39	2,400
120 grams bacon B	0.38	0.03	600
2,000 cubic centimeters coffee	1.04	0.32	
400 grams sugar			1,600
24 grams phytin		10.62	
20 capsules	0.75		
Total intake	28.21	14.80	7,250
Per day	7.05	3.70	1,810

	Total.		Per day.	
	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.
	Grams.	*Grams.*	*Grams.*	*Grams.*
Outgo, urine	21.99	5.25	5.50	1.31
Outgo, fæces	13.54	11.54	3.36	2.89
Total	35.53	16.79	8.86	4.20

	Balance.	
	Nitrogen.	P_2O_5.
	Grams.	*Grams.*
Intake per day	7.05	3.70
Outgo per day	8.86	4.20
Balance	**−1.81**	**−0.50**

PERIOD D.—*January 22 to 25, 1910.*

Food.	Nitrogen.	P_2O_5.	Calories (estimated).
	Grams.	*Grams.*	
800 grams rice I	10.56	2.44	2,650
1,050 grams bread	13.55	1.22	2,100
120 grams bacon B	0.38	0.03	600
1,500 cubic centimeters coffee	0.78	0.24	
400 grams sugar			1,600
24 grams phytin		10.62	
20 capsules	0.75		
Total intake	26.02	14.55	6,950
Per day	6.51	3.64	1,740

	Total.		Per day.			Balance.	
	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.		Nitrogen.	P_2O_5.
	Grams.	*Grams.*	*Grams.*	*Grams.*		*Grams.*	*Grams.*
Outgo, urine	22.12	4.37	5.53	1.09	Intake per day	6.51	3.64
Outgo, fæces	15.00	12.36	3.75	3.09	Outgo per day	9.28	4.18
Total	37.12	16.73	9.28	4.18	Balance	**−2.77**	**−0.54**

PERIOD E.—*January 26 to 29, 1910.*

Food.	Nitrogen.	P_2O_5.	Calories (estimated).
	Grams.	*Grams.*	
800 grams rice I	10.56	2.44	2,650
1,200 grams bread	15.48	1.39	2,400
1,000 cubic centimeters coffee	0.52	0.16	
200 grams bacon C	0.82	0.06	1,000
400 grams sugar			1,600
4 capsules	0.15		
Total intake	27.53	4.05	7,650
Per day	6.88	1.01	1,910

	Total.		Per day.			Balance.	
	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.		Nitrogen.	P_2O_5.
	Grams.	*Grams.*	*Grams.*	*Grams.*		*Grams.*	*Grams.*
Outgo, urine, 2 days	10.97	2.81	4.39	0.70	Intake per day	6.88	1.01
Outgo, urine, 2 days	6.60						
Outgo, fæces	14.83	2.62	3.71	0.66	Outgo per day	8.10	1.36
Total	32.40	5.43	8.10	1.36	Balance	**−1.22**	**−0.35**

PERIOD F.—*January 30 to February 2, 1910.*

Food.	Nitrogen.	P_2O_5.	Calories (estimated).
	Grams.	*Grams.*	
400 grams rice I	5.28	1.22	2,650
400 grams rice II	4.76	2.28	
1,200 grams bread	15.48	1.39	2,400
200 grams bacon C	0.82	0.06	1,000
600 cubic centimeters coffee	0.31	0.10	
360 grams sugar			1,440
36 grams egg albumen I	4.91		180
12 grams egg albumen II	1.63		
4 capsules	0.15		
Total intake	33.37	5.05	7,670
Per day	8.34	1.26	1,920

	Total.		Per day.			Balance.	
	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.		Nitrogen.	P_2O_5.
	Grams.	*Grams.*	*Grams.*	*Grams.*		*Grams.*	*Grams.*
Outgo, urine	23.92	3.36	5.98	0.84	Intake per day	8.34	1.26
Outgo, fæces	17.79	3.16	4.45	0.79	Outgo per day	10.43	1.63
Total	41.71	6.52	10.43	1.63	Balance	-2.09	-0.37

PERIOD G.—*February 3 to 5, 1910.*

Food.	Nitrogen.	P_2O_5.	Calories (estimated).
	Grams.	*Grams.*	
800 grams rice II	9.52	4.56	2,650
1,200 grams bread	15.48	1.39	2,400
400 grams sugar			1,600
400 grams fish (salmon)	15.12	1.68	500
3 capsules	0.12		
Total intake	40.24	7.63	7,150
Per day	10.06	1.91	1,790

	Total.		Per day.			Balance.	
	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.		Nitrogen.	P_2O_5.
	Grams.	*Grams.*	*Grams.*	*Grams.*		*Grams.*	*Grams.*
Outgo, urine	29.13	4.53	7.28	1.13	Intake per day	10.06	1.91
Outgo, fæces	13.42	3.65	3.36	0.91	Outgo per day	10.64	2.04
Total	42.55	8.18	10.64	2.04	Balance	-0.58	-0.13

SOME OBSERVATIONS CONCERNING BERIBERI.[1]

By Gorosaku Shibayama.[2]

(From the Institute for Infectious Diseases, Tokio.)

Marked attention has been given in Japan to the question of the etiology of beriberi since the Russo-Japanese war, not only in medical circles, but also in a practical manner. During the war, Japan had 200,000 cases of beriberi in the army, and this was the only ravaging epidemic with which the army had to contend. A beriberi commission, consisting of bacteriologists, pathologists, chemists and clinicians was therefore formed two years ago by the ministry of war, and I was one of the commission, who, together with two colleagues, made a journey to the Netherlands East Indies in order to observe the occurrence of beriberi in that region.

Beriberi is now very widely distributed in Java and Sumatra, much more so than in former years. The disease is present among a number of Chinese on the Island of Banka, where the tin mines are situated. We made a number of observations in this locality, which I wish briefly to mention in this place.

The present views concerning the etiology of beriberi are very diverse, and this is not the place to enter more extensively into a discussion of the literature, but the theory of the relation of the disease to the consumption of rice must here be considered. Ten years ago Eykman conducted some experiments with fowls, producing polyneuritis by the exclusive feeding of husked (polished) rice, whereas the unhusked (red) variety did not produce this result. Vordermann then demonstrated, in conformity with this work, that beriberi is a much rarer disease in prisons in Java where unhusked rice is used than in institutions in which the polished grain is employed. However, I wish to caution against regarding polyneuritis of fowls as being identical with human beriberi, and the observations of Vordermann leave many lapses and have much to be brought against them. Beriberi, as a fact, is endemic among oriental peoples who also use rice as the chief article of diet, and therefore the theory of the connection of the disease with the consumption of rice is always brought to the fore. The observations of Braddon, Fletcher, Ellis and Fraser, in the Malay Peninsula, have again called attention to this matter. According to the observations of these English authors, the consumption of parboiled rice is able to prevent the outbreaks of beriberi in hospitals and the disease can even be cured by the ingestion of this variety.

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, at Manila, March 11, 1910. Translated from the German by P. C. F.

[2] Delegate from His Imperial Japanese Majesty's Government.

Upon the basis of the theory of the connection of rice with the etiology of beriberi, a freshly husked, but not polished, rice was used in some of the mines on Banka Island, but the result was in evident contradiction to the theory.

In 1908, 1,195 cases of beriberi developed in the Blinjoe, one of the mining districts. Mine No. 3 was especially unfortunate, for 166, out of 410 workmen contracted the disease, and mine No. 4 developed 118 cases among 390. No. 5 had 400 workmen, and 97 of these were ill with beriberi; on the other hand, the remaining mines showed but few cases. For two years the workmen had received unpolished, fresh rice, not only in mines Nos. 3, 4, and 5, but also in No. 11, in which latter 49 out of 300 workmen contracted the disease; on the other hand, the laborers in the remainder always had polished and old rice. It may further be stated, according to Hullshoff-Pol, that the workmen in all the mines received 150 grams *kadjang idjo* beans, together with dried fish and fresh vegetables, daily. The result of our observations, therefore, was as follows:

1. Even if the workmen in the mines receive 150 grams of *kadjang idjo* regularly every day, nevertheless beriberi occurs among them.
2. Even if the laborers are given a diet of fresh, unpolished rice, nevertheless they develop more cases of beriberi than those in the other mines, where they receive polished and older Java rice.

I therefore could not find the assumption to be confirmed that unpolished rice, which has the same composition as parboiled rice, could prevent beriberi.

I wish to add some statements concerning a general epidemic on board a steamship which took 600 emigrants from Yokohama to South America; and 62 of whom were for various causes returned to that port with the same vessel. The entire voyage out and home took one hundred and thirty-nine days. Beriberi gradually appeared among the returning emigrants and by the time they reached Yokohama all, without a single exception, had contracted the disease, and 6 died. The remainder, upon arrival in port, were transferred to a hospital, where I saw the patients, and after a careful examination I proved that the sickness was genuine beriberi.

The question has not been decided as to whether the general epidemics which at times occur on board ship and which so greatly resemble beriberi are in reality always genuine beriberi, or only a similar condition or a scorbutic disease brought about through lack of nourishment. The Norwegian commission, in expressing an opinion concerning the beriberi of sailing ships, believed the disease to be genuine beriberi, whereas other authors, for example, Nocht in Hamburg, maintain that the condition is dependent on defect in nourishment. In my case, at least, the disease was genuine beriberi.

Furthermore, in the past summer, I observed an epidemic of beriberi in certain fishing villages of Japan.

All my observations lead me to the conclusion that uniform, but little changing, monotonous diet predisposes to the disease. The condition of nourishment of the Chinese in two of the mines of Banka was fairly good, the total quantity of the chief constituents of diet, namely, protein, fat and carbohydrates, was sufficient, but the diet was always one-sided and not varied throughout the year. This is also true of the general epidemic of beriberi aboard the steamship referred to above, and in the fishing villages the one-sided diet was the only point to be observed.

However, the one-sided or monotonous diet is only the predisposing cause of beriberi; the true cause must be sought in other directions. This can be illustrated by an example. Abdominal typhoid is treated in Europe and America, as well as in Java, or for that matter in the entire Orient, by means of a liquid diet, especially milk. In the Orient, beriberi very frequently occurs as a complication among the convalescent patients; whereas this has never been observed in Europe or America. It is also true in the Orient that during sieges of cities and under other circumstances where there is insufficiency of diet, beriberi is very frequently observed, whereas this is not the case in the Occident. It is therefore not unreasonable to assume that the microörganisms of beriberi are only present in the Orient and, given a predisposing cause, are capable of causing the disease, whereas in the West beriberi does not appear, owing to the absence of the infecting organisms, although the same favorable predisposing cause may be present.

FOOD SALTS IN RELATION TO BERIBERI.[1]

By E. D. KILBOURNE.[2]

Beriberi has probably existed in the Philippine Islands since very early times. Schneider[3] reported cases at Zamboanga in 1852. Koeniger[4] is, I believe, in error, in stating that beriberi did not exist among the natives prior to 1882, although it was probably less common than it is now. During and since the year 1877 the imports of rice have greatly exceeded the exports. From our present knowledge of the etiologic relation of polished rice to beriberi, it is safe to say that the disease was not absent during these and during previous years when the imports were not inconsiderable.

TABLE I.—*Imports and exports of rice into Manila, in kilos.*

Year.	Imported.	Exported.	Year.	Imported.	Exported.
1851–1857	None.	Not known.	1884	108,431,626	1,609
1858	1,393,040	772,920	1885	42,440,640	749
1859	746,460	820,440	1886	61,798,722	18,585
1860	1,758,240	6,313,428	1887	79,987,973	32,337
1861	16,218	2,443,500	1888	82,445,441	374
1862–63	Not known.	Not known.	1889	85,417,158	905
1864	1,046,100	20,396,300	1890	71,166,714	13,426
1865	253,257	21,650,046	1891	72,664,363	None.
1866	4,788	6,000,054	1892	62,709,137	254
1867	480,804	2,036,696	1893	41,000,503	62,492
1868–1872	Not known.	Not known.	1894	44,870,685	1,513,658
1873	7,311,002	13,278	1895–1897[a]	Not known.	Not known.
1874	10,811,589	101,371,178	1898–99[b]	55,817,073	None.
1875	2,910,847	1,524,855	1899–1900	110,141,537	None.
1876	239,539	3,571,931	1900–1901	178,605,867	None
1877	23,005,946	86,800	1901–2	216,812,362	None.
1878	23,670,099	265,285	1902–3	307,835,856	None.
1879	58,818,165	89,848	1903–4	330,518,006	None.
1880	13,555,647	366,241	1904–5	250,037,430	None.
1881	5,558,047	203,977	1905–6	138,341,469	None.
1882	8,971,305	840	1906–7	112,985,635	None.
1883	54,414,683	50,361	1907–8	162,515,826	None.

[a] No Spanish records could be found at the custom-house later than 1894.

[b] The American records begin with August 20, 1908, and show the amounts in the fiscal years ending June 30.

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, in Manila, March 11, 1910.

[2] Captain, Medical Corps, United States Army, Member of the United States' Army Board for the Study of Tropical Diseases as They Exist in the Philippine Islands.

[3] *Geneesk. Tijd. v. Ned. Ind.* (1890), **30**, 438.

[4] *Deutsches Arch. f. klin. Med.* (1884), **34**, 419.

Beriberi has been endemic among the native population since the occupation of the Philippines by the American forces in 1898, and several cases have been reported among the whites. Although I have examined several white soldiers and civilians, said to have beriberi, I can not say that I have ever seen a genuine case in this class, and am of the opinion that the disease is extremely rare among them. In the Tropics it is easy to confuse multiple neuritis from other causes with true beriberi.

The relationship of rice to beriberi is so well established that a consideration of one must include the other; therefore, a brief outline of the rice-eating habits of the inhabitants of the Islands is here given. Nearly all the tribes of the Philippines are of the Malay race, and though not all are of the same religious belief, their modes of preparing rice for eating are practically identical. None, as far as I can ascertain, use parboiled rice. There are a considerable number of Chinese and a few East Indians all of whom use polished rice, either native or imported. The latter prefer an Indian polished rice, which they import in small amounts for their own consumption.

The inhabitants of the interior use irrigated rice, when practicable, and mountain or upland rice when water is not accessible. Those in the lower lands, for the greater part, consume irrigated native rice. The inhabitants of the coastal plains use the latter, or imported rice brought, principally, from the British and French East Indies and from Siam.

For twenty-one years preceding, and since the American occupation, there has not been enough native rice produced to supply the population. Before 1877 this was not so; then the rice exported exceeded that imported. The various sources and amounts of rice imported since the American occupation are given in the following table, compiled from the records of the Bureau of Customs.

TABLE II.—*Sources of imported rice—fiscal years ending June 30—weights in kilos.*

Year.	United States.	United Kingdom.	France.	Spain.	Japan.	British East Indies.	Dutch East Indies.	French East Indies.	Siam.	Other Asia.
1899	--------	--------	--------	859,272	5,727	3,172,052	--------	6,774,902	--------	--------
1900	--------	--------	--------	6,619	129	5,589,964	--------	149,999,369	--------	--------
1901	--------	505	82	136,405	147	4,624,958	7,500	161,647,368	12,188,900	--------
1902	218,298	--------	--------	16,713	85,421	22,819,860	1,919	179,719,833	13,414,080	700,780
1903	6,665	--------	--------	42,040	8,258	27,687,089	--------	262,930,276	16,481,171	630,354
1904	--------	--------	--------	30,859	--------	38,443,895	29,547	264,317,216	(a)	26,519,980
1905	--------	--------	100	19,381	7,287	18,432,723	198,535	208,772,632	(a)	28,606,778
1906	--------	--------	--------	25,872	9,837	8,412,494	1,376	120,312,056	(a)	9,988,451
1907	--------	--------	--------	17,901	11,616	971,600	--------	106,673,410	5,311,105	--------
1908	--------	--------	--------	35,773	31,398	1,209,207	2,739	152,799,236	8,427,425	--------

[a] Siam rice 1904–1906 is included in that from "Other Asia."

The rice used in the Philippines, as regards preparation, is of three kinds: That grown at home and pounded out by hand in large wooden mortars; that grown at home and submitted to milling of varying degrees of thoroughness; and the imported rice, all of which has been milled and polished abroad.

The first variety, home grown and hand produced, is used in the rural districts and by about one-half of the natives in the coast towns. The second and third varieties, polished native and imported rice, are used principally in the coast towns and their immediate vicinity. There are regions where little or no rice is consumed, as in the Batan Islands, just north of Luzon. Meat and vegetables constitute the diet of the inhabitants of these islands; they have no beriberi. In the town of Aparri, 120 miles south of the Batan group, imported polished rice is found for sale in the *tiendas* and beriberi exists among the natives. On the contrary, in the coast towns of Casiguran and Baler, which are around the northeastern corner of Luzon from Aparri, no imported rice was observed in the *tiendas* and no beriberi among the people.

In general, beriberi is found in the coast towns and along the lines of communication, and in the same places polished rice is extensively eaten. At Taytay, in Rizal Province, a small town of 6,000 inhabitants about 15 miles from Manila, beriberi is remarkably infrequent, although the town is on the railroad. As a matter of fact, however, polished rice seems to be used there little, if any. Samples of rice gathered at random in the *tiendas* of Taytay were all of the home-grown varieties and incompletely milled.

Our observations seem to prove that beriberi in the Philippines is found only where polished rice, either imported or home grown, is used, principally along the coasts or rivers. No doubt the new railway system will open up increased areas where polished rice will be consumed and the distribution of beriberi in the Philippine Islands may be changed in the next few years.

This etiologic relation of polished rice to beriberi agrees with the findings of other workers. If polished rice is a factor in the causation of beriberi, and this seems to us to be proved, it must be because it either conveys into the body some extraneous poisonous substance, or else is deficient in, or, at least, fails to give to the body enough of some needed element or elements. The work done in the Philippines by Major Dutcher and others, and our own observations, have failed to give any support to the first idea, consequently our researches have been directed to an investigation of the privation theory.

It is not sufficient to make deductions from analyses of the various rices, polished and parboiled, or to draw conclusions from experiments in which such rices are fed to lower animals, although such experiments may be suggestive and point out a profitable line of research in the human. The ingestion by the human of other articles of diet, rich in a certain element, may entirely compensate for the lack of such element in the rice eaten, so unless the entire diet of a body of men for a period equal, at least, to the so-called "period of incubation" is known, no reliable conclusions can be drawn. From the analysis of one predominating article of food we might conclude that the Irish peasant has this or that disease because the potatoes, which constitute a large part of his diet, contain a very small percentage of phosphorus. If we examine his entire ration we find that this element is amply supplied by milk and eggs, which are easily and cheaply obtained. Eykman[4] and Sakaki[5] have shown that fowls fed on polished rice develop polyneuritis in five to ten weeks, but horses develop a condition akin to beriberi[6] when fed on unhusked grain, the food which prevents the condition in the case of the fowls. We have no means of knowing that these diseases in animals are caused by the same conditions that induce human beriberi. Monkeys, in our laboratory, fed on boiled, polished rice and water alone, showed no bad effects for fourteen weeks and actually gained in weight.

To determine in what respect the diets containing a considerable proportion of polished rice are at fault, the United States Army Board for the Study of Tropical Diseases as They Exist in the Philippines, of which I am a member, has, during the past year, studied the situation as it exists in the native troops (Philippine Scouts). To obtain reliable and accurate data from the civilian natives is impossible; only in a military organization, prison, school, or other similar body is it possible to exercise a control sufficient to make the findings of any value. Consequently, our observations on the civilian population are of a general nature only and made from material incidentally gathered while working on beriberi among the Scouts.

The Scouts were organized in 1901. The annual reports of the Surgeon-General of the United States Army first mention beriberi as occurring among individuals of this body of troops in 1902.

Beriberi in the Philippine Scouts.

Year.	Admissions per 1,000.	Deaths per 1,000.	Year.	Admissions per 1,000.	Deaths. per 1,000
1902	7.75	0.38	1906	36.98	1.79
1903	9.42	.37	1907	24.58	1.28
1904	74.62	1.52	1908	121.58	1.35
1905	35.93	1.21			

In 1909 the admissions of scouts to sick report, because of beriberi, were only exceeded in number by two other causes, malaria and miscellaneous digestive troubles.

It was evident, after a study of the data obtained from the records of these companies, that the amounts of proteid, fat and carbohydrate actually consumed were sufficient.

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[4] Polyneuritis bij Hoenders. *Geneesk. Tijd. v. Ned. Ind.* (1896), 36.

[5] *Sei-i-Kwai* (1903), March 31, April 30.

[6] Braddon, W. L. The Cause and Prevention of Beriberi. (1907), 350.

The Filipino ration (issued to the Scouts) is as follows:

Component articles.	Quantities.	Substitutive articles.	Quantities.
	Ounces.		*Ounces.*
Beef, fresh	12	Bacon	8
		Canned meat	8
		Fish, canned	12
		Fish, fresh	12
Flour	8	Hard bread	8
Baking powder (in field)	0.32		
Rice	20		
Potatoes	8	Onions	8
Coffee, roasted and ground	1		
Sugar	2		
Vinegar	[a] 0.08		
Salt	0.64		
Pepper	0.02		

[a] Gill.

A considerable latitude is allowed in the amounts consumed. For example: If the company does not care to use a certain article of food on the ration list, it need not draw it from the commissary, but will in its place receive a commuted value, in cash, at the end of the month, with which to purchase other articles from outside sources. Also, the company may have a substantial "company fund" derived from its share of the profits of the post exchange and post bakery with which to buy desired articles of food to enrich the mess. When the company is stationed in an inaccessible place, away from markets, it must necessarily live almost entirely from the commissary; but when quartered near good markets it may be able to buy fresh vegetables and other things cheaply and draw little from the commissary. In these ways the ration actually eaten by the men may differ considerably from that laid down by the Army Regulations.

To determine exactly what the dietaries were, the company and subsistence department records were consulted and the actual articles and amounts ascertained. In no case were the amounts of proteid, fat and carbohydrate found deficient. The Filipino ration, as listed, contains approximately the following: Proteid, 122 grams; fat, 45 grams; carbohydrates, 685 grams. The proteid and fat are ample, and the amount of carbohydrates is more than enough for a Filipino who weighs about four-fifths as much as the average American.

In recent years the rôle played by the inorganic salts in the human economy has been given a great deal of study. In the last decade much work has been done by physiologists on the action of salts on the healthy organism, but the relation of the different salts to known pathologic conditions has only partially been worked out.

The principal salts introduced with the food are combinations of chloride are found in the garrison ration, there are only 1.3 in that of the Filipino troops, a remarkable difference. An average of 1.6517 grams was found in our third or beriberi-free group.

An important influence of the potassium salts has been noted by Bunge.[12] "If a potassium salt be in solution together with sodium chloride, the two partially react on each other, with formation of potassium chloride. If now potassium carbonate, for example, be eaten, the same reaction occurs in the body: $K_2CO_3 + 2NaCl \leftrightarrows 2KCl + Na_2CO_3$. The kidney has the power of removing soluble substances which do not belong to the blood, or are present in it to excess, and consequently the two salts formed as above are excreted. Hence, potassium carbonate has caused a direct loss of sodium and chlorine. For this reason, if potatoes and vegetables rich in potassium salts are eaten, sodium chloride must be added to the food to compensate for the loss. Natives living on rice do not need salt, for here the potassium content is low. Tribes living solely on meat or fish do not use salt, but care is taken that the animals slaughtered for food shall not lose the blood rich in sodium salts, and strips of meat dipped in blood are, by some races, considered a delicacy." If this be true, an excess of sodium salts will cause a loss of potassium in the same manner.

Jaques Loeb[13] has shown the necessity for a balance between the Na, Ca, and K ions, and that the Ca and K ions counteract the effects of the Na ions in the blood. When marine animals were placed in a pure solution of sodium chloride of the same concentration as sea water, their muscular contractility was lost. Small amounts of Ca and K ions antagonized the poisonous effects of the Na ions.

Herter gives the daily amount of sodium chloride necessary for a man as about 8 grams, which would be about 6.5 grams for a Filipino. The average daily amount of table salt consumed by each man in the organizations we investigated was 10 grams. This amount, ordinarily not harmful, since most people consume quantities far in excess of the physiological requirements, might be too much for diets as low in K ions as are those of the Scouts.

The amounts of calcium ingested were greatly in excess of their physiological needs.

The necessity of a proper balance in food salts is shown by the relation of varying amounts of sodium chloride to the œdema of nephritis, and of calcium chloride to epilepsy and rickets.

A deficiency in the amounts of potassium and phosphorus, or a disproportion between these elements and sodium, calcium and magnesium, might well account for the production of beriberi. As in the case of rickets and scurvy, because of the intricacy of the problems involved, and the large part played by the selective powers of the body tissues, we may never be able to express in terms of chemical equations the pathologic processes of this disease, but I believe we do know enough of its etiology to prevent its occurrence.

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[12] Physiologische Chemie. 3. ed. (1894), 108–116.

[13] *Am. Journ. Phys.* (1900), 3, 327.

By a proper diet we hope to eradicate it from the native troops. Of course, predisposing causes, such as bad ventilation, overexertion, exposure, etc., must receive their share of attention. As a result of our studies, certain changes are to be instituted in the Filipino ration. The rice is to be reduced to 16 ounces and native No. 2 rice substituted for the polished Siam grain now supplied. One and six-tenths ounces of beans are to be added. It is hoped, that by these changes beriberi will disappear from the Scouts.

DISCUSSIONS ON THE PAPERS BY DOCTORS DE HAAN, FRASER, HIGHET, ARON, SHIBAYAMA, AND KILBOURNE.

Dr. Gilbert E. Brooke, port health officer, delegate from the Straits Settlements, Singapore.—I assure every one that I am very glad to have heard this series of papers, which shows how much careful work has been performed on this subject. That the removal of the outer covering of the rice grain is one of the causes of beriberi seems, from what we have heard, to be probable, the phosphorus content being reduced. However, I must say that it appears to me that we must be careful not to jump too hastily at conclusions. Before we can accept such a conclusion as this we should inquire into many other factors, for one, concerning the occurrence of beriberi in countries in which the principal diet is not rice, and another, its nonappearance in countries where rice does form the principal food. Another question is concerning the phosphorus content of other foods, which counterbalances the lack of phosphorus in white rice. The natives of this part of the world use fish wherever it is obtainable and fish contains phosphorus. Doctor Kilbourne, in his paper, states that beriberi was present in the Philippine Islands in 1882, but it seems unreasonable to assume that the natives at that time were already eating polished rice. They probably had the same diet as at present. Doctor Highet said that previous to 1890 white rice was quite expensive in Siam. I should like to ask him whether steam-milled rice had been exported from that country.

I have looked over the records for thirty years, covering the admission of cases of beriberi into the hospitals of the Straits Settlements and these develop the fact that no cases of the disease, or at least very few, occurred before 1878. Beriberi began to appear about the year 1880 and afterwards increased. We have had a considerable number of cases of beriberi annually from 1879 up to the present time. We began to use steam-milled rice in Singapore in 1890. There was no beriberi in Singapore jail from 1896 to 1897. The prisoners were given rice found in the market, which is the food of the native population, and the latter also had beriberi.

I had an opportunity of seeing the beginning of a case of beriberi taken from the quarantine station in Singapore. We had a number of hospital attendants, Chinese, who lived in barracks. They were doing the work of nurses. In October, 1896, we lacked one man. We secured a person about 31 years of age. He lived with the other coolies. They had separate rooms, but they all ate the same food. Until December 25 none of these assistants went to Singapore. We allowed very little visiting, but permitted them to go once a month for a period of twenty-four hours. On December 25 this new man had 24 hours' leave and went to Singapore, but he returned the following morning. On January 5 this man complained of shortness of breath. I found him suffering from constriction of the chest; the following day his legs developed signs of weakness, on the seventh day he was very weak and on the eighth day he could no longer stand. I inquired concerning him on March 4 in order to discover what he had eaten during the twenty-four hours when he was in Singapore. I found that he had eaten two meals. I visited the house where he had eaten and found no beriberi there.

I bring this case to your attention so as to turn the latter on the possible origin of beriberi in this instance. There would seem to have been a short incubation period.

Dr. J. de Haan, director of the Government Medical Laboratory at Weltevreden, delegate from Her Majesty's Government of the Netherlands Indies.—Can Doctor Aron explain, by his view of the extraction of phytin, why the curative effect of *katjang idjo* is lost when the beans are heated to 120°?

Dr. Aldo Castellani, professor of tropical medicine and lecturer on dermatology, Ceylon Medical College, Colombo, delegate from the Government of Ceylon.—It was with great pleasure that I listened to these papers and to their discussion. I have always been strongly of the opinion that this matter should for the greater part be left to those who have especially worked with it; I have a certain amount of clinical experience with the disease; but have never undertaken any experimental work on it. The investigations of Doctors Fraser, Aron, and Kilbourne are, to my mind, the most convincing of all that I am aware of. In fact, I think that the supporters of the old theory of beriberi are in a very poor position; but I do not believe that the rice theory alone holds. I certainly agree with Doctor Aron that an insufficiently nutritrious diet may produce general debility, but may it not be that white rice and the general debility caused by its excessive consumption may render the individual more liable to be infected by the specific parasite causing beriberi? It seems to me that the rice theory does not explain the occurrence of the disease in some tropical countries and its absence in others. In Ceylon there are half a million Indian coolies who eat the same rice as those in India. In fact, the rice for our coolies is for the greater part imported from India; still, not a single case of beriberi has occurred in Ceylon.

In conclusion, I would ask to be allowed to express my admiration of the great work of Doctors Aron, Fraser, and Kilbourne.

Dr. Hans Aron, associate professor of physiology, Philippine Medical School.—In reply to Doctor de Haan's question, I will state that, in my opinion, it is probable that if by a process of sterilization the soluble phosphorus compounds and phytin from beans (such as *mongo*) or from rice are extracted, this fact would explain the deleterious action of, say, sterilized beans, etc. I did not venture to touch upon this subject in my paper because I did not have sufficient experimental data, but this explanation is very clear to anyone who has worked with the question. An important point in regard to the process of sterilization would be to discover if, by this means, any extracts are produced which are separated from the beans and lost. A recent paper from the Physiological-Chemical Institute in Strassburg demonstrates that bread, when extracted, can not sustain mice in normal health, but if the extracts are added to the extracted bread, or unextracted bread is fed to the animals, they remain in good health.

In reply to Doctor Castellani's question, I would say that it can not be denied that the deleterious action of white rice could be explained by the supposition that a diet of this variety might favor the development of certain infective organisms. I can not agree as to the validity of calculations such as those made by Doctor Kilbourne. In the first place, even under military discipline, it is not possible to control the amount which each individual actually takes when the amount given to, say, 100 men only is known. I have observed that stricter rules are in force in Bilibid Prison than in the United States Army, and that even the prisoners exchange certain portions of their food; thus one man will trade meat for rice; or milk for cigarettes, and so on. I observed the same thing in Culion, when on a trip with Doctor Heiser. *Mongo* and rice are issued in Culion, a certain number of pounds for a certain number of men, but one man might eat rice alone, because he did not like *mongo;* others would take *mongo* because they were afraid of an attack of beriberi which at that time was prevalent in the colony.

In the second place, errors would be made in calculating the composition of foodstuffs according to tables or text-books. My own analyses demonstrate the great differences in the composition of two classes of the same food-stuffs, especially of rice. I do not know how anyone can determine the phosphorus content from the appearance of the rice alone. It is for these reasons that I doubt the value of such calculations, fraught as they are with two such grave errors.

Dr. Isaac W. Brewer, Medical Reserve Corps, United States Army.—Major Ruffner, United States Army, has asked me to present the statistics from Camp Connell, which during the past year has been one of the largest stations for native troops in the Islands. One hundred and eight cases occurred at that post from May to October, 1909. The disease was eliminated by increasing the amount of beef, bread, and beans given in the rations, and by limiting the rice to one meal daily, which was taken at night. The entire command was examined every second Sunday and all suspicious cases were taken into the hospital so that the statistics are complete. The quality of the rice was not changed during this period.

Doctor de Haan.—I wish to reply to Doctor Castellani's objection to the view that the etiology of beriberi is due to the rice consumed, by the statement which I mentioned in my paper, namely, that neither in the blood nor the organs of men suffering from *Polyneuritis epidemica* nor in the organs of those who have died of this disease nor in the blood or organs of fowls suffering from experimental polyneuritis have antibodies or antigen been found. It is therefore improbable that an infection by microbes is the cause of beriberi, since we know that in all such infections antigen or antibodies are produced as a result of reaction by the infected organisms.

Dr. Gorosaku Shibayama, Institute for Infectious Diseases, Tokyo, delegate from His Imperial Japanese Majesty's Government.—It has been known for ten years that fowls, exclusively fed on polished rice, may contract polyneuritis, whereas the birds given the unpolished grain remain free from the disease. On the other hand, unpolished rice can produce polyneuritis when it has been heated to 120°. There is no chemical difference, especially in regard to the content of phosphorus, between heated and nonheated rice.

Furthermore, the occurrence of epidemics of beriberi in fishing villages has taught us that the inhabitants of the latter eat large quantities of fresh fish, and this diet contains, relatively, a large amount of phosphorus. We have treated many cases of beriberi with phytin, but we could not observe any very favorable results.

I would also, in this place, wish especially to emphasize the fact that the polyneuritis of fowls is not identical with beriberi, and that the experimental results obtained with these birds can not directly be interpreted in the same sense with human beings. So, for example, polyneuritis accompanies general cachexia and inanition in fowls, whereas beriberi, especially the acute, pernicious form, generally attacks well-nourished, muscular men.

Dr. Henry Fraser, director of the Institute for Medical Research, Kuala Lumpur, Federated Malay States, delegate from the Government of the Federated Malay States.—With reference to the observations of Major Kilbourne on the nutritive value of the diets issued to the people under his care, I do not think that we can estimate these from the composition of the various foodstuffs recorded in text-books because, in our experience, these records show considerable differences from the results of analyses carried out by us.

There are numerous species and varieties of rice; these differ in composition. Beef in the Tropics is poorer in fat and pork is richer in fat than the corresponding articles as generally met with in Europe. If, then, we are to derive any information from the composition of the diets in respect to proteins, fats, carbohydrates and salts, actual analyses of the foodstuffs as issued must be made.

In our work at Durien Tipus we analyzed all the foodstuffs issued, and on comparing the diet issued to the party on parboiled rice with that issued to the party on white rice, no really important differences were observed, and both diets, considered in this way, should have sufficed for the physiological requirements of the individual.

We believe in our work at Durien Tipus that we excluded the operation of every other factor save rice in the production of beriberi.

Comparison of the composition of parboiled and white rices showed differences in respect to fat and ash, but the difference in amount of fats could not account for the results if we consider these bodies merely as the esters of fatty acids. The difference in amount of ash we have shown to depend mainly on the phosphorus compounds. Further investigation is necessary to explain the significance of this.

I believe that the method of estimating diets from the amount of proteins, fats, carbohydrates and ash contained in them will require reconsideration and in all probability readjustment.

In the light of recent research this method has shown itself to be crude and incapable of showing differences which may be of vital importance to the physiological requirements of the individual. Doctor Aron's researches are of the greatest importance and shed a large amount of light on this difficult problem, but I doubt if the difference in respect of phytin will explain the results.

In the case of the parboiled and white rices used by us and both derived from the same kind of paddy, we have estimated the phosphorus pentoxide in the washed and dried rices, because the rices are washed previous to cooking.

Now if we consider all the phosphorus estimated in this way to be combined as phytin and that a man receives one and a third pounds of rice daily, we find that the men on white rice would receive about 1.5 grams of phytin daily and those on parboiled rice about 3 grams of this substance.

The matter is, however, one of scientific interest and at present of no practical importance to those engaged in the prevention of beriberi.

Our researches have conclusively shown that beriberi can be prevented by the use of unpolished rice and as surely produced by the use of highly polished rice.

We have furnished you with three methods by which it is possible to determine the liability or otherwise of a given rice to produce beriberi.

1. Chemical.
2. Histological.

3. By feeding experiments on fowls.

Of course, if the dietary of those peoples among whom beriberi is occurring be improved, the use of highly polished rice might be continued and no untoward effect occur, but so long as these peoples continue to partake of a diet in which rice constitutes the staple, our efforts must be directed to maintaining the rice at a standard sufficient for their physiological requirements.

I wish to correct here one misapprehension. It is not the removal of the pericarp which makes the rice harmful, but of the layers subjacent to the pericarp (subpericarpal layers); the cells composing those layers differ in respect of their constituents from the cells composing the central part of the endosperm.

Dr. H. Campbell Highet, principal medical officer local government, Bangkok, delegate from His Imperial Majesty's Government, Siam.—In discussing epidemics of beriberi in mines, the theory that arsenical poisoning may be the cause of the particular polyneuritis observed must not be forgotten. I can give no information with respect to how long white Siam rice had been imported into Singapore. As regards the one case of beriberi which arose amongst seven members of Doctor Brooke's quarantine staff, it should always be borne in mind that one swallow does not make a summer, and that this one case proved nothing. However, allowing that this case was really beriberi and that the symptoms appeared to develop after nearly three months' residence on the quarantine island, this was not remarkable. If we were to speak of such a thing as an incubation period, I could not fix any definite time for such a period. It may vary from a few days to months or even to a year or more. Why may Doctor Brookes's case not have been a relapse? Men with extended experience in beriberi know that before starting upon feeding experiments the investigator must be careful in the examination of the persons about to undergo treatment in order to eliminate old or incipient cases of the disease. My own experience is that beriberi once contracted is most difficult to eradicate entirely, and that months or even years afterwards some sudden strain upon the health might bring about a condition in every way like acute beriberi. A case of a Siamese police sergeant may be cited, who, after a prolonged residence in hospital, suffering from beriberi, returned to duty and did good work for eighteen months. Having had a dispute with one of his subordinates, he was put into a police cell to await trial. In thirty-six hours he became so ill that he was transferred to hospital, where he died in a few hours, with all the symptoms of acute, wet beriberi. On post-mortem examination, it was quite evident that the lesions of the heart were the result of prolonged illness. He had the largest "bullock's heart" I ever saw. His previous history was not known, but the conclusion might easily have been reached that this was a case of acute, wet beriberi whereas it was simply a relapse in a very chronic case.

Dr. H. M. Neeb, medical officer of the first class, delegate from Her Majesty's Government of the Netherlands Indies.—I wish to ask Doctor Shibayama if, in his investigations of the cases observed in the Island of Banca, in the mines, where fresh rice was given, he made sure that there were not previous cases or relapses. It is true that patients who have had beriberi and recovered therefrom, so as apparently to be in a healthy condition, a long time afterwards if suddenly placed in bad surroundings, for instance, violent change of climate or excessive hard labor, will not infrequently suffer a relapse. If, now, patients are given fresh, unpolished rice, it might appear, if they contract beriberi, as if this food were the cause, whereas there may be nothing but a relapse produced by other conditions and not by the rice.

In regard to the question of beriberi on sailing ships, I wish to state that about a year ago Professor Nocht studied two cases where men had died from this cause. Doctor Rodenwaldt examined pathologic-anatomic preparations of the spinal cord and peripheral nerves and found the changes to be quite the same as those which occur in exotic beriberi, so that Professor Nocht has come to the opinion that both varieties of beriberi are identical.

Kakke (beriberi) has been termed *Polyneuritis epidemica* during this discussion, but investigations in Japan have demonstrated, to a certain extent, that the alterations in the nerves are mainly secondary degenerations, the principal change being in the vascular system. For that reason the symptom complex differentiating *kakke* (beriberi) and intoxication polyneuritis is easy to determine. I do not wish to confuse beriberi with the polyneuritis of intoxication.

Dr. E. D. Kilbourne, captain, medical corps United States Army, member of the United States Army Board for the Study of Tropical Diseases as they exist in the Philippine Islands.—In reply to Doctors Aron and Fraser I will state that the amounts of phosphorus and potassium shown in the table were average amounts taken from a large number of men over a period of several months. Although the figures may not be absolutely correct, they are of value in showing the relative amounts of phosphorus and potassium in the three groups, and show a greater reduction in potassium than phosphorus in the affected groups. The phosphorus and potassium contents of various foods used to compute the tables were themselves average figures taken from a number of different analyses, so the amounts given in the table are considered to be fairly correct. I fully appreciate the criticism which Doctor Aron makes of my calculations, but analyses of identical rice made in different laboratories show at least as great variations in composition as he states occur between different kinds of rice.

Dr. Francis Clark, medical officer of health, delegate from the Government of Hongkong.—In order to strengthen the hands of medical officers concerned in public health administration or in the medical supervision of native laborers, and after consultation with some of those attending this congress, I desire, after the discussion is closed, to move a resolution in regard to the formation of a committee on beriberi.

The wording is immaterial so long as you are prepared to confirm the principal involved, namely, that this disease is occasioned by the consumption of white or highly polished rice as the staple article of diet. The adoption of such a resolution will yield a practical issue to the discussion and will enable us to take early steps to protect the natives under our care from a disease which is responsible for much suffering and many deaths.[1]

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[1] The following resolution was finally passed by the association (Ed.):

"*Resolved*, That in the opinion of this Association sufficient evidence has now been produced in support of the view that beriberi is associated with the continuous consumption of white (polished) rice as the staple article of diet, and the Association accordingly desires to bring this matter to the notice of the various Governments concerned."

REVIEW.

Retinitis Pigmentosa. With an Analysis of Seventeen Cases in Deaf-Mutes.—By William T. Shoemaker, M. D. Laboratory Examinations of the Blood and Urine, by John M. Swan, M. D. Cloth. Pp. IV+106. Price $2. 1st ed. Philadelphia: J. B. Lippincott Company.

This little book on retinitis pigmentosa gives an exceedingly satisfactory discussion of the subject. The description of the pathology, symptoms and fundus changes are concise and yet complete. The plates are beautiful and anyone able to view the fundus should, with their aid, have no trouble in making a diagnosis even in a first case.

The author's statement that the disease is particularly prevalent in the Orient should interest practitioners in this region and induce them to investigate closely any complaint of night-blindness by patients. This symptom with contraction of the visual fields and the retinal pigmentation make the disease "one of the most easily recognized in the domain of ophthalmology."

Doctor Shoemaker's conclusions may be briefly summarized as follows:

1. That the disease is a degeneration, not an inflammation, of the entire neurovascular tract of the peripheral end-organ of vision.
2. That the retinal changes are secondary to changes in the choroid.
3. That the disease is congenital in all cases, however long the symptoms may be delayed, and that it may be considered as a stigma of degeneracy.
4. That heredity is a potent etiologic factor; parental consanguinity is of importance only in connection with heredity and environment; maternal impressions can not be excluded as a possible cause; and syphilis as a cause of true retinitis pigmentosa is not established.
5. That the distribution is of more importance than the mere presence of retinal pigment in making the diagnosis.
6. That the disease is *always* bilateral.

R. P. O'C.

NOTICE.

Beginning with the January, 1910, issue the old-established Medical Review of Reviews will be edited by Dr. William J. Robinson, editor and founder of the famous Critic and Guide, Therapeutic Medicine, and The American Journal of Urology.

The editorial offices of the Medical Review of Reviews have been removed to 12 Mt. Morris Park W., New York City.

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THIS NUMBER CONTAINS PAPERS READ AT THE FIRST BIENNIAL MEETING OF THE FAR EASTERN ASSOCIATION OF TROPICAL MEDICINE, HELD AT MANILA, MARCH 5 TO 14, 1910.

THE PHILIPPINE
JOURNAL OF SCIENCE
B. MEDICAL SCIENCES

VOL. V JULY, 1910 No. 2

STUDIES ON INFANT MORTALITY.[1]

By ALLAN J. MCLAUGHLIN[2] and VERNON L. ANDREWS.[3]

The death rate among Filipinos in Manila, as shown below, is excessive compared with that of other nationalities, after making due allowance for the higher birth rate, greater proportion of children, and other factors.

TABLE I.—*Death rate in Manila by nationalities, per thousand, during the year 1909.*

Spaniards	12.05
Americans	13.27
Other Occidentals	14.32
Chinese	16.64
Filipinos	47.65

This enormous death rate is due to the high mortality of children. Of 9,307 deaths among the Filipino population, 6,041, or 64.9 per cent, were of children under 5 years of age, and 4,542, or 48.8 per cent, were of infants under 1 year of age.

TABLE II.—*Rate of infant mortality to total number of deaths.*

Total number of deaths, all ages	9,307
Total number of deaths under 5 years	6,041
Total number of deaths under 1 year	4,542
Rate of deaths under 1 year to total number, per cent	48.8

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[1] Read at the First Biennial Meeting of the Far Eastern Association of Tropical Medicine, March 9, 1910.

[2] Passed Assistant Surgeon, United States Public Health and Marine-Hospital Service; Assistant Director of Health for the Philippine Islands; and assistant professor of Hygiene, Philippine Medical School.

[3] Assistant, Biological Laboratory, Bureau of Science, and Assistant Professor of bacteriology and pathology, Philippine Medical School.

Compare this infant mortality with that of other countries and the result is striking. According to the United States census of the year 1900, the deaths of children under 1 year constitute 18.28 per cent of the total mortality; in France,[4] from 1896 to 1900, the infant mortality constituted 20 per cent of the total, but in Manila the deaths of infants under 1 year aggregate 48.8 per cent of the total number.

TABLE III.—*Rate of deaths of children to total number of deaths, in percentages.*

United States	18.28
France	20.00
Manila	48.8

In order to combat intelligently this appalling infant mortality, it is essential to determine accurately what diseases really constitute the greatest factors and these investigations were undertaken with that end in view.

According to the statistics of the Bureau of Health, the main factors in child mortality for the fiscal year 1908–9, a fairly representative year, were the following:

TABLE IV.—*Factors in the mortality of children in Manila.*

Cause of death.	Number of deaths, children under 1 year.	Number of deaths, children under 5 years.
Convulsions	1,615	1,615
Congenital debility	596	596
Beriberi	595	629
Acute bronchitis	569	689
Acute meningitis	287	510
Enteritis	286	745
All other causes	594	1,257
Total	4,542	6,041

It was necessary to verify these statistics. The figures for the total number of deaths were undoubtedly correct, but the causes given in the death certificates were demonstrated frequently to be incorrect and indefinite.

In a previous paper, one[5] of us presented some observations upon cholera in children during the period from August 1 to September 25, 1909, and among the conclusions deduced from those observations were the following:

1. Cholera in children is often unrecognized and unreported as such, the diagnosis being reported as acute or chronic enteritis, gastroenteritis, enterocolitis,

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[4] Budin. *Ann. de Med. et chir. infant* (1903), 7, 181.

[5] McLaughlin. Some Observations Upon Cholera in Children. *This Journal, Sec. B* (1909), 4, 363.

dysentery, acute or simple meningitis and probably also as infantile beriberi, convulsions of children, and some other forms of disease.

2. Cholera in children is often atypical, and in these cases diagnosis is extremely difficult, if not impossible, without bacteriological examination of the intestinal contents.

3. Cerebral manifestations in children suffering from cholera are very common and their severity is in inverse proportion to the age of the child.

4. Acute meningitis is a very rare disease in Manila, in spite of statistics.

5. The percentage of children attacked by cholera is higher than is shown by statistics.

In our work we are able to confirm the conclusions expressed above in regard to meningitis and cholera, and to present additional data bearing upon infantile beriberi, convulsions of children, enteritis, bronchitis and broncho-pneumonia. The clinical history as gleaned from the family or attending physician is given in the tables. These histories are meager and are not always reliable, owing to the fact that the case is often seen late in the disease and to the difficulty of getting correct data from the family. However, it is unlikely that all the histories are unreliable, particularly as the unanimity is so marked.

In all cases of meningitis, beriberi, convulsions and bronchitis the necropsy findings are given. In the cases of enteritis and dysentery, necropsies were not performed in every instance, and confirmation of the diagnosis of Asiatic cholera was secured by bacteriologic examination of the intestinal contents at the Bureau of Science.

ACUTE MENINGITIS.

The following table shows the deaths from acute meningitis in Manila by months for the past nine years:

TABLE V.—*Acute meningitis in Manila from 1901 to 1909, inclusive.*

Month.	1901	1902	1903	1904	1905	1906	1907	1908	1909
January	26	21	17	25	28	22	23	78	33
February	24	21	14	26	16	23	23	92	32
March	56	28	17	24	26	30	22	44	34
April	21	25	14	25	34	32	28	31	27
May	29	50	30	32	24	35	37	35	24
June	22	54	13	47	27	40	23	45	48
July	15	34	17	51	31	95	27	93	31
August	27	39	36	40	34	70	34	64	40
September	33	25	43	49	58	40	53	62	27
October	28	34	41	50	32	25	58	54	4
November	25	29	33	30	24	26	43	46	2
December	25	32	26	36	24	30	50	45	3
Total	331	392	301	435	358	468	421	689	305

Average number of cases per year, 410; average number of cases per month, 34.

These statistics cover nine full years, and from them it will be noticed that the average number of deaths from meningitis in Manila was about 410 per year, or 34 per month. The investigation by necropsy of children dead from alleged meningitis began the last week of September, 1909. The number of deaths from meningtis recorded for October dropped to 4, for November to 2, and for December to 3.

Table VI, opposite page 160, shows the cases of alleged acute meningitis which came to necropsy, together with the clinical data and pathologic findings.

The following is a summary:

Summary of Table VI.

Acute meningitis	2
Pneumonia	2
Empyema	1
Beriberi	10
Cholera	18
Undetermined (not meningitis)	3
Enterocolitis	1
Total	37

ACUTE ENTERITIS AND OTHER DIARRHŒAS.

Tabue VII, opposite page 160, gives an analysis of a number of cases of alleged enteric disease.

We wish to emphasize the fact that diagnosis in these cases was difficult, or impossible from the clinical symptoms and that the examination of the intestinal contents should be compulsory in all children acutely sick in Manila. In these instances the classical symptoms of cholera were either absent or overlooked, because of their transient character. Sometimes the choleraic signs present were masked by intercurrent diseases and the predominance of cerebral manifestations.

Summary of Table VII.

Cholera	15
Beriberi	2
Pneumonia	2
Enterocolitis	3
Total	22

INFANTILE CONVULSIONS.

The diagnosis "infantile convulsions" should not be accepted as a cause of death. It is only a symptom of some specific disease and has no more right to a place in statistics than fever or chills. Table VIII, opposite page 160, shows the results obtained from investigations by necropsy of cases of alleged infantile convulsions, with clinical data and pathologic findings.

Summary of Table VIII.

Beriberi	31
Cholera	4
Pneumonia	1
Enterocolitis	1
Empyema	1
Cerebral hæmorrhage	1
Undetermined	1
Total	40

The importance of securing correct diagnoses in the cases reported as dying of infantile convulsions is at once evident in view of the fact that 35 per cent of the total mortality under 1 year is given on the death certificates as being due to this cause. In accepting these reports we admit that the real cause of 35 per cent of the mortality in Manila of infants under 1 year of age is unknown to us.

BRONCHITIS.

Table IX, opposite page 160, shows the results of necropsies on 27 cases in which the death certificate gave acute or chronic bronchitis, or bronchopneumonia as the cause of death. Some of the bodies were in bad condition when they came to autopsy, owing to warm weather supervening and the difficulty of transferring them to the morgue with sufficient promptness.

Summary of Table IX.

Beriberi	14
Pneumonia	6
Meningitis	2
Nephritis	2
Chronic colitis	1
Acute tonsilitis, pharyngitis and bronchitis	1
Undetermined	1
Total	27

INFANTILE BERIBERI.

Table X, opposite page 160, gives the results in cases of alleged infantile beriberi. The first cases of so-called infantile beriberi which we investigated in November proved to be of Asiatic cholera, and we were at that time somewhat doubtful of the existence of the former disease in infants and rather expected that our experience with alleged acute meningitis would be repeated. Further study showed that a large number of infants die of a disease which presents a definite pathologic picture for which we know no better name than "moist beriberi."

Summary of Table X.

Beriberi	40
Cholera	3
Broncho-pneumonia	3
Enterocolitis	1
Undetermined	3
Total	50

In the pathological entity which we have called "beriberi" we come face to face with one of the real factors in Filipino infant mortality. This disease is responsible for many more deaths than would appear to be the case from statistics. We have found not only that many instances of alleged congenital debility and convulsions are due to beriberi, but also acute bronchitis and pneumonia. It is our opinion that the two diseases last mentioned are not common, and an investigation of deaths from acute bronchitis and broncho-pneumonia shows many of them to be due to beriberi.

The clinical symptoms of dyspnœa and cardiac embarrassment are often responsible for a diagnosis of bronchitis, or broncho-pneumonia, when the necropsy reveals the picture of beriberi. While we recognize the fact that bronchitis is a disease of childhood and old age, we hardly think that the figures as given in Table IV for bronchitis state the truth. It seems to us that the number of children under 1 year is too large and that the difference between 1 year and 5 is too small. True, it is in early infancy that the disease is most marked and it is more prevalent in squalid homes and among poorly nourished infants than elsewhere, yet we doubt if this would account for the figures as given.

A summary of the 176 cases studied is given in Table XI.

TABLE XI.—*Showing the number of cases investigated, together with clinical diagnoses and necropsy findings.*

Clinical diagnoses.		Necropsy findings.	
Meningitis	37	Cholera	40
Enteritis	22	Beriberi	97
Convulsions	40	Pneumonia	14
Beriberi	50	Enterocolitis	7
Bronchitis	27	Meningitis	4
		Nephritis	2
Total	176	Empyema	2
		Acute tonsilitis, pharyngitis and bronchitis	1
		Cerebral hæmorrhage	1
		Undetermined	8
		Total	176

The great discrepancy between the clinical diagnoses and the autopsy findings can partially be explained by the fact that in many instances the native doctor is not called to see the patient until the latter is moribund, or, in some cases, until after death, and the family want a death certificate signed.

In 1898 and 1900, Professor Hirota,[6] of Tokyo, described a disease found in some infants brought to his clinic, which he called infantile beriberi. A few years later, 1905 (?), the native doctors of Manila and the Philippines accepted Hirota's findings and began signing death certificates giving the cause of death as infantile beriberi. So far as the writers know, no effort was made by the native physicians to establish by necropsy any relation between the findings of Hirota in Tokyo and the disease called infantile beriberi by the Filipinos. For some reason, the subject has never been taken up by the American physicians in the Islands, owing, possibly, to the fact that they do not come in contact with the poorer Filipinos, and hence are never called upon to treat them. In the various hospital dispensaries the children are looked after by the native doctors. A number of Filipino physicians have recognized the condition here and one[7] has described a typical case with necropsy.

In the pathologic entity which we have termed "infantile moist beriberi," and for which we know no better name, we find the following conditions:

The body is that of an apparently well-nourished infant, plump; skin is usually pale and anæmic. The face is full, with almost a swollen appearance. Flesh of thighs and legs is soft and flabby and, as a rule, pits on deep pressure. Occasionally the skin has a tough, leathery feel, a leaden color and a slight gooseflesh appearance.

Subcutaneous fat is present, apparently in good amount, grayish-white in color and very moist; muscles are anæmic. Owing to the œdema, the real amount of fat present is deceptive and hence the bodies may not be as well nourished as they appear.

Most often there is an increase of peritoneal fluid, which has a distinct yellowish color.

Heart.—The pericardial sac is filled with a clear fluid, having a greenish tint. Probably the most striking and constant change is found in the right heart. Its musculature is coarse and firm and forms much the larger part of the organ, even in the contour of the apex. Its trabeculæ and papillary muscles are prominent, while its cavity is enlarged. The wall of the right ventricle may measure from 5 millimeters to 7 millimeters in thickness, whereas the left measures only 3 millimeters to 5 millimeters. (See Plate I.) The musculature of the left heart is soft and flabby and darker than that of the right. The blood vessels of the heart are congested and prominent and frequently a few hæmorrhages show along the auriculo-ventricular junction. In many cases the foramen ovale is still patulous, but is competent.

Lungs.—These organs are a light pinkish-gray anteriorly and a light purplish-gray posteriorly. They fill the pleural cavities and crepitate throughout. The anterior part of the lung is lighter and more fluffy than the posterior. Few or many petechial hæmorrhages may show beneath the visceral pleura, especially along the junction of the lobes. Occasionally there is a slight increase of the pleural fluid.

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[6] *Centralbl. f. inn. Med.* (1898), 19, 385; *ibid.* (1900), 21, 273.

[7] Albert. *This Journ., Sec. B* (1908), 3, 345.

A cut section shows a pinkish-gray surface, which may or may not exude some blood. Air can be expressed from all portions of the lung and usually also a slight amount of œdematous fluid. The posterior part of the lung is of a darker color and is heavier than the anterior and more fluid can be expressed from it than from the anterior part. The bronchi do not appear to be hyperæmic, but contain more or less frothy material and mucus. Sometimes this can be expressed from the smaller bronchi.

Spleen.—This organ may be very hyperæmic and show slight increase of splenic tissue, partially obliterating the normal markings.

Kidneys.—The kidneys are of a reddish-gray color, fœtal lobulations are prominent. A cut section is very moist and a considerable amount of blood oozes from it. Striations of the cortex are plainly seen. Except for congestion, the kidneys, in the greater number of cases, present a normal appearance. Occasionally a slight degree of albuminous degeneration, or a few subcapsular hœmorrhages occur. The adrenals show congestion.

Liver.—The liver is dark reddish-brown in color and firm. Section shows congestion and rarely a slight "nutmeg" appearance is seen. The lobulations are usually clearly defined. Here, also, we may find some albuminous degeneration.

Stomach.—The stomach nearly always contains some curdled milk and mucus. The mucosa is smooth and anæmic. No rice or other artificial food was found in the stomachs of any of the cases; sometimes there is a trace of fæcal material present.

Intestines.—They are normal in appearance. The intestinal contents are semiliquid, apparently digested, and have a yellow color. The mesenteric glands may be slightly enlarged and soft.

Urinary bladder.—It may or may not contain urine.

Throat organs.—Except for some froth and mucus present in the larynx and trachea, these organs are normal.

Thymus.—The thymus is usually prominent and full. Some milky fluid can almost always be expressed from the cut surface.

Meninges and brain.—The meninges are congested and œdematous, and there is usually an increase of the cerebro-spinal fluid. The brain substance may be of normal consistency, or soft and very moist.

Many of the bodies were not subjected to necropsy until twenty-four or thirty-six hours after death, because of our inability to transport them to the morgue at a sufficiently early time, and in this warm climate decomposition very rapidly sets in. However, in the above description of the gross pathology three points are prominent: First, the dilated and hypertrophied right heart; second, the congestion of all internal viscera; third, the anasarca. The two last conditions naturally follow the first, and we turn to the lungs for a possible explanation. Microscopically they present a varied condition, being in part emphysematous and the more dependent portions being heavily congested, with the alveoli filled with epithelial cells, leucocytes, and granular œdematous material. In some places small hæmorrhages have occurred and the red cells are found in the alveoli and tissues.

In this paper we do not attempt to give the etiology of the condition. A microbic origin for it is not excluded, as we have not been able to enter upon this phase of the investigation because of the length of time elapsing between the death of the patient and the time of necropsy, and the press of other work; but if the condition is of microbic origin, its manifestation is entirely different from that produced by other organisms that we know. There is no inflammatory focus in the lungs or elsewhere.

Clinically, the cases were not seen by either of us, and all the information we have was obtained by the medical inspectors and is contained in the tables. The inspectors give the history that the patient is sick but a few hours, or, at most, but a day or two. The parents, however, do not recognize that the child is ill until its condition is very serious, or until it is almost dead. The probability is that it has been ailing for some time, possibly since its birth.

Nearly all of the infants examined were under 2 months of age, and but few were above 2½ months old. Almost without exception they were breast fed, and in no case was rice or other artificial food found in the stomach. The mothers in nearly all instances exhibited some symptoms of beriberi. Many of them give the history of having two, three, or even five or more children die from similar symptoms. The disease is well known among the native poor, who call it *"taon"* or *"suba"* (propably the latter is the more common name), and who dread it very much.

In a careful analysis of the pathologic findings by necropsy in a series of 219 infants dying under 1 year of age, we found the above-described condition, which, for want of a better term, we have designated as "moist beriberi," to be present in 124 cases. The following summary gives an analysis of all of those cases.

Table showing results of necropsies on 219 infants 1 year of age or under.

Beriberi	124
Cholera	33
Pneumonia	18
Meningitis	6
Enterocolitis	6
Other diseases	20
Undetermined [8]	12
Total	219

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[8] In some of the undetermined cases the findings were obscured by post-mortem decomposition; other bodies were greatly emaciated and death seemed to be due to a lack of assimilation of food.

This table includes all the cases discussed in the preceding investigations under the headings meningitis, enteritis, convulsions, bronchitis and beriberi, excepting a few cases of meningitis over 1 year of age, which were excluded. The total was increased by including some necropsies made during March and April, after the other investigations were concluded.

The table indicates that "beriberi" (?) is the largest factor in the infant mortality of Manila, and the existence of this factor accounts in great measure for Manila's excess in infant mortality over that of other countries, as shown by Table III. Cholera appears because the investigations were begun during a mild epidemic of that disease in Manila. Tubercular meningitis was found twice and tuberculosis of the lungs once. This does not indicate the measure of the prevalence of tuberculosis among Filipino infants, as deaths from this disease were not investigated.

GENERAL CONSIDERATIONS.

The infant mortality of Manila presents a striking contrast to that of other cities. The deaths of breast-fed children constitute 73.74 per cent of the total infant mortality; furthermore, 87 per cent of infants dying of beriberi and convulsions in Manila are breast fed. The following table shows the figures as compiled in the Bureau of Health for the year ending February 25, 1910.

TABLE XII.—*Showing per cent of deaths among breast-fed infants under 1 year, by disease.*

Diseases.	Number of certificates stating how fed.	Number breast-fed.	Per cent of breast fed to total reported on.
Beriberi	473	417	88.1 +
Convulsions	872	763	87.5
Acute bronchitis	615	469	76.2 +
Congenital debility	381	218	57.2 +
Meningitis	134	75	56 —
Enteric disease	201	70	34.8 +
Other diseases	722	494	68.4 +
Total	3,398	2,506	73.74+

In Munich, of 4,000 dead infants during 1903, 83 per cent were artificially fed;[9] in Berlin, in a period of five years, only 9 per cent of the infant mortality occurred in breast-fed babies.[10]

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[9] Wile. *Pediatrics* (1909), 21, 203.

[10] Graham. *Journ. Am. Med. Assoc.* (1908), 51, 1045.

TABLE XIII.—*Showing per cent of total infant mortality which occurs in breast-fed and artificially fed infants in different cities.*

City.	Breast-fed.	Artificially fed.
	Per cent.	*Per cent.*
Berlin	9	91
Munich	17	83
Manila	73.74	26.26

Tugendreich[11] states that in 64 families with 388 breast-fed children there had been 77 deaths, a mortality of 19.8 per cent. On the other hand, he found that 33 families with 229 bottle-fed children had 99 deaths, a mortality of 43.2 per cent. Twenty-four of the 64 families with 109 exclusively breast-fed children escaped without a single death, while not one of the 33 families with bottle-fed children escaped without the loss of at least one child. In other countries the mortality among breast-fed infants is very low.

In Germany, France, or the United States a breast-fed infant means a healthy infant in 90 per cent of the cases, because the mothers in those countries are usually healthy and well nourished. In the Philippines the mortality is greatest among breast-fed children, possibly because of the poor quality of the mother's milk. The latter is probably deleterious by reason of what it lacks rather than because of any harmful constituent. The average Filipino mother is in poor physical condition, many of them are beriberic and subsist upon a diet favorable to beriberi. It seems probable that there is an intimate relation between beriberi of infants and a mother's milk poor in quality and lacking certain necessary elements which are not included in the mother's dietary. At first glance it might seem advisable to supplant breast feeding by artificial, but under existing conditions this would be a blunder. The children saved from beriberi would be sacrificed to enteric diseases. That small part of our infant population which is artificially fed furnishes 65 per cent of the deaths from enteric diseases, and the breast-fed, much the larger part of the population, furnishes but 35 per cent of the infant mortality from this cause; so that even in Manila, breast-feeding of infants exerts a deterrent influence upon the mortality from gastrointestinal diseases. A possible solution of the problem lies in improving the quality of the mother's milk and encouraging the continuance of the custom of breast-feeding so general among the Filipino poor. The improvement of the physical condition of the Filipino mother and of the quality of her milk is an economic question. Her condition is the result of poverty and therefore insufficient and unsuitable food, especially during the periods of pregnancy and lactation.

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[11] *Arch. f. Kinderheilk.* (1908), 48, 390.

However, it must be remembered that the etiology of this disease is unknown. Clinically, the cases must be observed by competent men under favorable conditions where a complete clinical record can be made. The sick ones should be taken to a hospital where they can be studied carefully and all laboratory and biologic tests applied. The careful examination of all body fluids and excreta, biologically and chemically, is imperative. Further, the possibility of an ultramicroscopic organism must not be overlooked, neither should the internal secretions be forgotten. At the same time, a thorough chemical and biologic examination of the mother's milk is essential. At death a quick necropsy with complete biologic examination must follow. This would also give material for thorough histologic study, which has been impossible so far because of post-mortem changes.

The writers wish to extend their thanks to Dr. H. Winsor, of St. Paul's Hospital, for performing some of the autopsies.

TABLE VI.—*Cases of alleged meningitis.*

Case.	Clinical data.								Pathologic findings.											
	Age. y. m. d.	Convulsions or convulsive symptoms.	Rigidity of neck.	Strabismus.	Fever	Collapse.	Vomiting.	Rice water diarrhœa.	External appearance of cholera.[a]	Subcutaneous tissues.	Peritoneum.	Heart.	Lungs.	Spleen.	Kidneys.	Liver.	Intestines	Meninges and brain.	Anatomic diagnosis.	Bacteriologic diagnosis.
1	3 – –	Yes	No	No	Slight	No	No	No	Yes	Dry	Dry	Normal	Congestion	Normal	Nephritis	Albuminous degeneration	Slight congestion.	No inflammation	Cholera	Cholera.
2	2 4 –	No	Yes	Yes	Yes	No	No	Fæculent diarrhœa	Yes	do	do	Right, dilated	Congestion and œdema	do	Albuminous degeneration	do	Congestion	Congestion	do	Do.
3	– 10 –	Yes	No	Yes	Yes	No	Nausea	Yellow diarrhœa	Yes	do	do	do	do	do	Nephritis	do	Inflamed	Congestion, œdema	do	Do.
4	1 – –	Yes	No	Yes	Yes	No	No	No	Yes	do	do	do	do	do	do	Congestion	do	do	do	Do.
5	1 – –	Yes	No	Yes	Yes	No	No	Constipation	Yes	do	do	do	Congestion	do	do	do	do	do	do	Negative.
6	3 – –	No	No	Yes	High	No	No	No	Yes	do	do	do	do	do	Congestion	Albuminous degeneration	do	do	do	Cholera.
7	3 – –	Yes	Yes	No	No	Cold extremities	Yes	Yes	Yes	do	do	do	do	do	Nephritis	Congestion	do	Congestion	do	Do.
8	– 6 –	No	No	Slight	Yes	No	No	No	Yes	do	do	do	do	do	Congestion	do	do	Congestion, œdema	do	Negative.
9	3 – –	Yes	Yes	No	Yes	No	No	No	No	Moist	Moist	Normal	do	do	Nephritis	Normal	Normal	Suppurative congestion	Suppurative meningitis	Do.
10	– 10 –	No	No	No	Slight	No	No	Fæculent diarrhœa	No	do	do	do	Normal	do	Normal	do	do	Normal	Undetermined[b]	Do.
11	– 5 –	Yes	Yes	No	Yes	No	No	Yellow-diarrhœa	No	do	do	do	Pneumonia	Congestion	Nephritis	do	do	Congestion	Pseudo-lobar pneumonia[b]	No report
12	– 3 –	Yes	No	No	Yes	No	Yes	do	No	Dry	Dry	Soft	Congestion	Normal	Normal	do	do	Congestion, œdema	Undetermined	Negative.
13	2 – –	Yes	No	Yes	Yes	No	No	No	Yes	do	do	Right, dilated	do	do	Nephritis	do	Inflamed	Congestion	Cholera	Cholera.
14	3 6 –	Yes	No	No	High	No	No	Yellow, liquid stools	Yes	do	do	do	Congestion and œdema	do	Congestion	Congestion	do	No inflammation	do	Negative.
15	– 8 –	No	Slight	Yes	Slight	No	Nausea	No	Yes	do	do	do	Congestion	do	Albuminous degeneration	Albuminous degeneration	do	do	do	Cholera.
16	1 1 –	Yes	No	No	High	No	do	Greenish yellow stools	Yes	do	do	do	do	do	Congestion	do	do	Congestion	do	Do.
17	– 8 –	Yes	No	No	Slight	No	No	Greenish-yellow liquid stools.	Yes	Post-mortem decomposition									Undetermined[c]	Do.
18	5 7 –	Slight	No	No	Yes	No	No	No	Yes	Dry	Dry	Right, dilated	Congestion	Normal	Albuminous degeneration	Albuminous degeneration	Inflamed	No inflammation	Cholera	Do.
19	– 4 –	Yes	Yes	Yes	Yes	No	No	No	Yes	do	do	do	do	do	do	do	do	Congestion	do	Do.
20	8 – –	Yes	No	No	Yes	No	No	No	Yes	do	do	do	do	do	do	do	do	No inflammation	do	Do.
21	1 – –	No	No	No	Slight	No	No	No	Yes	do	do	do	do	do	do	do	Congestion	Congestion	do	Do.
22	– 11 –	No	No	No	Yes	No	No	No	No	Slight œdema.	Ascites	Right, dilated and hypertrophied	do	Congestion	do	do	Normal	Normal	Beriberi	Negative.
23	5 – –	Yes	No	Yes	Yes	No	No	No	No	Moist	do	do	Congestion and œdema	do	Congestion	do	do	Congestion	do	Do.
24	– 8 –	Yes	No	Ptosis	Yes	No	Yes	No	No	do	Moist	do	Congestion	Normal	Albuminous degeneration	do	Slight congestion	do	do	Do.
25	– 2 –	Yes	Yes	Yes	Yes	No	No	No	No	do	do	do	Broncho-pneumonia	Congestion	do	do	do	do	do	Do.
26	– 4 –	Yes	Yes	Yes	High	No	No	No	No	Firm	Normal	Dilated and hypertrophied	Empyema	do	Congestion, albuminous degeneration	do	Normal	Suppurative meningitis	Meningitis	Do.
27	– 9 –	No	No	Yes	High	No	No	No	No	do	Moist	do	Congestion	do	Albuminous degeneration	do	do	Congestion	Beriberi	Do.
28	– 11 –	Yes	Yes	Yes	Yes	No	Nausea	No	Yes	Dry	Dry	Right, dilated	Congestion and œdema	Normal	Congestion	Congestion	Inflamed	Congestion, œdema	Cholera	No report.
29	– 10 –	Yes	No	Yes	Yes	No	Yes	Soft, yellow stools	No	Moist	Ascites	Right, dilated and hypertrophied	do	Congestion	Albuminous degeneration	Albuminous degeneration	do	do	Beriberi	Negative.
30	– 7 –	Yes	No	No	Yes	No	No	do	No	Firm	Normal	Normal	Congestion	do	Normal	Congestion	Normal	Slight congestion	Empyema	Do.
31	– 9 –	Yes	Yes	Yes	Yes	No	Yes	No	No	Moist	Ascites	Right, dilated and hypertrophied	do	do	Congestion	do	do	Congestion, œdema	Beriberi	Do.
32	2 7 –	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Dry	Dry	Right, dilated	do	Normal	Albuminous degeneration	Albuminous degeneration	Inflamed	Congestion	Cholera	No report.
33	4 – –	No	No	No	Yes	No	No	No	No	Moist	Moist	Normal	Pneumonia	do	Congestion	Congestion	Congestion	do	Pneumonia	
34	– 2 –	Yes	No	Yes	Yes	No	Yes	Yellow	No	Firm	Ascites	Right, dilated and hypertrophied	Congestion, œdema	Congestion	do	do	Normal	Congestion, œdema	Beriberi	
35	– – 10	No	No	No	Yes	No	Nausea	No	No	Moist	Moist	do	Congestion	Normal	Congestion, albuminous degeneration	Congestion, albuminous degeneration	do	Normal	do	
36	– 8 –	Yes	No	No	Yes	No	No	No	No	do	Ascites	do	Congestion and œdema	Congestion	do	do	do	Congestion, œdema	do	
37	– 4 5	Yes			Yes	No	No	No	No	Dry	do	Normal	Congestion	Normal	Congestion	do	Inflamed	Normal	Acute colitis	

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[a] By external appearance of cholera the writers have reference to a picture presenting the following: A haggard drawn expression of the face with sunken, half open eyes. The finger nails are bluish in color, the skin of the fingers is shriveled and wrinkled, and the skin covering the body is drawn and tight, as a rule.

[b] Greatly emaciated infant, death probably due to nonassimilation of food.

[c] Post-mortem decomposition.

TABLE VII.—*Cases of alleged enteritis and other diarrheas.*

Case.	Clinical data.									Pathologic findings.											
	Age.	Fever.	Vomiting.	Collapse.	Urine.	Character of diarrhea.	Convulsions or convulsive symptoms.	Dyspnea and cyanosis.	Clinical diagnosis.	External appearance of cholera.	Subcutaneous tissues.	Peritoneum.	Heart.	Lungs.	Spleen.	Kidneys.	Liver.	Intestine.	Meninges and brain.	Anatomic diagnosis.	Bacteriologic diagnosis.
	y. m. d.																				
1	5 – –	Yes	No	No	Abundant.	Fetid, dark	No	Yes	Typhoid fever	Yes	Dry	Dry	Normal	Congestion	Normal	Congestion	Albuminous degeneration	Inflamed	Congestion	Cholera	Cholera.
2	4 – –	Yes	No	No		Mucus and blood	No	Yes	Acute dysentery	Yes	do	Sticky exudate	do	do	do	Albuminous degeneration	do	do	Normal	do	Negative.
3	– 1 –	Yes	Yes	No	Scanty	Greenish, pasty	No	No	Acute enteritis	Yes	Moist	do	Right dilated	do	Congestion	do	do	do	do	do	Cholera.
4	– 1 –	No	Once	Yes	Sufficient.	Yellow	No	Yes	Acute gastroenteritis	Yes	Dry	Dry	do	do	do	do	do	do	Congestion	do	Do.
5	– 3 –	No history obtainable							Acute enteritis	No	Moist	Ascites	Right dilated and hypertrophied			Congestion			do	Beriberi	Negative.
6	– 6 –	do							do	Yes	Dry	Dry	Normal	do	Congestion	do	Congestion	Inflamed	Normal	Cholera	Do.
7	1 – –	Yes	Yes	No		Greenish-yellow	No	Slight cyanosis.	Chronic gastroenteritis	Yes	do	do	Right dilated	do	Normal	Albuminous degeneration	Albuminous degeneration	do	Congestion	do	Do.
8	6 – –	Yes	No	No		Mucus and blood	No	No	Acute dysentery	No necropsy; specimen of intestinal contents taken after death											Cholera.
9	1 6 –	Yes	No	No		Greenish stools	No	Slight	Acute gastroenteritis	do											Do.
10	2 – –	Yes	Yes	No	Scanty	Light yellow	No	No	Acute enteritis	Case recovered; diagnosis from stool specimen											Do.
11	2 – –	Yes	No	No	Normal	Feculent	No	No	Acute gastroenteritis	do											Do.
12	2 – –	Yes	Yes	No		do	No	No	do	No necropsy; specimen of intestinal contents taken after death											Do.
13	3 – –	Slight	No	No	Normal	do	No	No	Chronic tubercular enteritis	do											Do.
14	3 6 –	Yes	No	No		Mucus and blood	No	No	Acute dysentery	do											Do.
15	1 – –	No clinical history obtainable							Acute enteritis	No	Moist	Moist	Normal	Pneumonia	Normal	Albuminous degeneration	Albuminous degeneration	Normal	Normal	Lobar pneumonia	No report.
16	1 9 –	do							Acute gastroenteritis	Yes	Dry	Dry	Right dilated	Congestion	do	Congestion	do	Inflamed	do	Cholera	Cholera.
17	– 5 –	do							Chronic gastritis	No	Moist	Moist	Right dilated and hypertrophied	do	do	do	Normal	Normal	Congestion	Beriberi	Negative.
18	– – 27	do							Acute gastroenteritis	No	do	do	Right dilated	Pneumonia	Congestion	do	do	do	do	Pneumonia	No report.
19	– 6 –	Yes	Yes	No			Yes	Yes	do	Yes	Dry	Dry	do	Congestion	do	Congestion, albuminous degeneration	Albuminous degeneration	Inflamed	do	Cholera	
20	1 – –	Yes					Yes		do	No	do	Moist	Normal	Congestion and œdema	do	Congestion	do	do	Normal	Acute enteritis	
21	– 4 –					Mucus			Undetermined	No	do	Dry	do	Œdema	do	Albuminous degeneration	Congestion	do		Acute enterocolitis.	
22	– 10 –	Yes	Yes		Plentiful	Dysentery			Chronic gastritis	Yes	do	do	do	Normal	Normal	do	Albuminous degeneration	do	Congestion, œdema	do	

TABLE VIII.—*Cases of alleged infantile convulsions.*

Case.	Clinical data.								Pathologic findings.											
	Age.	Convulsions or convulsive symptoms.	Fever.	Collapse.	Vomiting.	Diarrhœa.	Dyspnœa and cyanosis	Urine.	External appearance of cholera.	Subcutaneous tissues	Peritoneum.	Heart.	Lungs.	Spleen.	Kidneys.	Liver.	Intestines	Meninges and brain.	Anatomic diagnosis.	Bacteriologic diagnosis.
	y. m. d.																			
1	2 – –	Yes	Yes	No	No	Yes	No		Yes	Dry	Dry	Normal	Congestion œdema	Normal	Albuminous degeneration	Albuminous degeneration	Inflamed	Normal	Cholera	Cholera.
2	– 1 –	Yes	No	No	No	No	Yes	Amount normal	No	Moist	Moist	Right dilated and hypertrophied	do	do	Congestion	Congestion	Normal	Congestion	Beriberi	
3	1 – –	Yes	No	Cold extremities	Yes	Yes	Slight	do	Yes	do	Slight ascites	Normal	Œdema	Congestion	do	do	Congestion	Normal	Enterocolitis	Negative.
4	– 2 –	Yes	No	No	No	No	Yes		No	do	do	Right dilated and hypertrophied	Congestion, œdema	do	Albuminous degeneration	Albuminous degeneration	Normal	Congestion	Beriberi	Do.
5		No history obtainable							No	do	do	do	do	do	Normal	do	do	Normal	do	Do.
6	– 1 13	Yes	No	No	No	Yellow	Yes	Diminished	No	do	Moist	do	do	do	Nephritis	do	do	Congestion	do	Do
7	– 1 10	Yes	No	No	No	No	Yes	do	No	do	Slight ascites	do	Congestion	Normal	Congestion	do	do	Normal	do	Do.
8	– 2 –	Yes	No	No	No	No	Yes		No	do	Ascites	do	Congestion, œdema	Congestion	do	Congestion	do	do	do	Do.
9	– 2 13	Yes	No	No	No	Yellow	No	Amount normal	Yes	Post-mortem decomposition									Undetermined[a]	Do.
10	– – 27	Slight	No	No	No	No	No		No	Moist	Moist	Right dilated and hypertrophied	Congestion	Congestion	Congestion	Congestion	Normal	Normal	Beriberi	Do
11	– 3 12	Yes	Yes	No	No	No	Yes	Diminished	No	do	Slight ascites	do	do	do	do	do	do	Congestion	do	Do.
12	– 1 15	Slight	No	No	No	No	No		No	do	Moist	do	Congestion, œdema	do	do	do	do	do	do	Do.
13	– 1 8	No	Yes	No	No	No	No		No	do	Slight ascites	do	Congestion	Normal	Nephritis	Albuminous degeneration	do	Normal	do	Do.
14	– 2 –	Yes	No	No	Yes	Greenish liquid	No	Amount normal	No	do	do	do	Congestion, œdema	Congestion	Normal	do	do	Congestion	do	Do.
15	– 2 –	Yes	No	No	No	No	Yes		No	do	do	do	Congestion	do	Albuminous degeneration	do	Slight congestion	do	do	
16	– 2 –	No	No	No	No	No	Yes	Diminished	No	do	do	do	do	Normal	Congestion	Congestion	Normal	Œdema	do	
17	– 2 –	No	No	No	No	Greenish liquid	Yes	do	No	do	Moist	do	do	do	Albuminous degeneration	do	do	do	do	Do.
18	– 1 9	Yes	No	No	No	Yellow		Suppressed	No	do	do	do	do	do	Normal	Albuminous degeneration	do	Congestion	do	Do.
19	– 7 –	Yes	No	No	No	No	Yes	Diminished	No	do	do	Purulent pericarditis	Pneumonia	Congestion	Albuminous degeneration	do	do	do	Pneumonia	Do.
20	– 6 26	Yes	No	No	No	No			No	do	Slight ascites	Right dilated and hypertrophied	Congestion, œdema	Normal	Congestion	Normal	do	Œdema	Beriberi	Do.
21	– 1 25	Yes	No	No	No	Feculent	Yes	Amount normal	No	do	Moist	do	Congestion	Congestion	do	Albuminous degeneration	do	Congestion	do	Do.
22	– 6 15	Yes	Yes	No	Yes	Fetid greenish yellow	No	Not noted	No necropsy; specimens of intestinal contents taken after death											Cholera.
23	– 1 16	Yes[#]	Yes	No	No	No	No	do	do											Do.
24	– 8 11	Yes		No	No	No		do	No	Moist	Moist	Right dilated and hypertrophied	Post-mortem decomposition						Beriberi	Negative.
25	– 2 24	Yes	No	No	Yes	No	Yes	Diminished	No	Œdema	Ascites	do	Congestion	Normal	Congestion	Congestion	Normal	Œdema	do	Do.
26	– 3 25	Yes				No	Yes	do	No	do	do	do	do	do	do	do	do	do	do	Do.
27	– 3 16	Slight	No		No	No	Yes		No	Moist	Moist	do	do	do	do	Congestion, albuminous degeneration	do	Normal	do	Do.
28	– 1 –	Slight	No	No	No	No	Yes	Not noted	No	do	do	do	Congestion, œdema	Congestion	do	Congestion	do	do	do	Do.
29	– 2 –	Yes	No	No	Yes	No	Yes	Anuria	No	Œdema	do	do	Congestion	do	do	do	do	do	do	Do.
30	– 3 –	Yes	No	Yes	Yes	Slight	Yes	Normal	Yes	Dry	Dry	Right dilated	do	do	Albuminous degeneration	Albuminous degeneration	Inflamed	Congestion	Cholera	Cholera.
31	– 2 18	Yes		No	Yes	Slight			No	Moist	Moist	Right dilated and hypertrophied	do	do	Congestion	Congestion	Normal	Œdema	Beriberi	
32	– 1 8	Yes	Yes				Yes		No	Œdema	Ascites	do	Congestion, œdema	do	do	do	do	do	do	
33	– 1 –	Yes	Slight	No	Yes	Yes	Yes		No	Normal	Moist	Normal	Congestion, empyema(?)	Normal	Normal	Normal	do	Normal	Empyema	
34	– 5 14	Yes	No	No	No	No	Yes	Scanty	No	Œdema	do	Right dilated and hypertrophied	Congestion, œdema	Congestion	Congestion	Congestion	do	do	Beriberi	
35	– 1 15		No	No	No	No	Yes	Anuria	No	do	Ascites	do	do	do	do	do	do	Œdema	do	
36	– 2 10		No	No	No	No	Yes	Normal	No	do	do	do	do	do	do	do	do	Congestion, œdema	do	
37	– 1 25	Yes	No	No	No	No	Yes	Scanty	No	Moist	do	do	do	do	Albuminous degeneration	do	do	do	do	
38	– 1 14	Yes	Yes	No	Yes	Yes	Yes		No	Œdema	do	do	do	do	Congestion	do	do	Congestion	do	
39	– 2 5	Yes	No	No	No	No	Yes	Normal	No	Dry	Moist	Normal	Hemorrhage	do	Jaundiced	Jaundiced	do	Hemorrhage	Cerebral hemorrhage	
40	– 1 11	Yes	No	No	No	No	Yes		No	Œdema	Ascites	Right dilated and hypertrophied	Post-mortem decomposition						Beriberi	

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[a] Post-mortem decomposition.

TABLE IX.—*Cases of alleged bronchitis or broncho-pneumonia.*

Case.	Clinical data.									Pathologic findings.											
	Age.	Fever.	Cough.	Dyspnea.	Cyanosis.	Diarrhea.	Convulsions.	Beriberic symptoms in mother.	Feeding.	External appearance of cholera.	Subcutaneous tissues.	Peritoneum.	Heart.	Lungs.	Spleen.	Kidneys.	Liver	Intestines	Meninges and brain.	Anatomic diagnosis	Bacteriologic diagnosis.
	y. m. d.																				
1	— 1 —	Yes	Yes	Yes	Yes	No				No	Moist	Moist	Right dilated and hypertrophied	Œdema	Normal	Congestion	Congestion	Normal	Congestion	Beriberi	
2	— 4 —	Slight	Yes	Yes	Yes	No			Breast	No	do	Ascites	do	Congestion, œdema	Congestion	do	do	do	Congestion, œdema	do	
3	— 1 7	No	Yes	Yes	Yes	No	Yes	Yes	do	No	do	Moist	do		Normal	Albuminous degeneration	Albuminous degeneration	do		do	
4	— — 15	Yes		Yes	Yes	No	Yes	No	do	No	Firm	Normal	Normal	Broncho-pneumonia		Post-mortem decomposition				Broncho-pneumonia	
5	— — 15	Yes	Yes	Yes	Yes	No	Yes	No	do	No	Œdema	Ascites	Right dilated and hypertrophied	Congestion, œdema	Normal		Congestion	Normal	Congestion, œdema	Beriberi	
6	— 5 13	Yes	Yes	Yes	Yes	No	Yes	Yes	do	No		do	do			Post-mortem decomposition				do	
7	— 11 —	Yes	Yes	Yes	Yes	No		No	Mixed	No	Firm	do	Normal	Œdema	Normal	Congestion	Albuminous degeneration	Normal	Meningitis	Suppurative meningitis	
8	1 1 —	Yes	Yes	Yes	Yes	Yes	Yes	No	Artificial	No	do	Normal	do	Pneumonia	do	Albuminous degeneration	do	do	Congestion œdema	Lobar pneumonia	
9	— 10 —	Yes	Yes	Yes	Yes	No	No		do	No	do	do	do	do		Post-mortem decomposition				Broncho-pneumonia	
10	— 6 7	Yes	Yes	Yes		No		No	do	No	do	do	do	Œdema	Normal	Nephritis	Normal	Normal	Normal	Acute nephritis	
11	— 1 8	Yes	Yes	Yes	Yes	No	No	No	Breast	No	Œdema	Ascites	Right dilated and hypertrophied	Congestion, œdema	Congestion	Congestion	Congestion	do		Beriberi	
12	— 4 3	Yes	No	Yes		No	Yes	No	do	No	Firm	Normal	Normal	Œdema	Normal	Albuminous degeneration	do	do	Meningitis	Suppurative meningitis	
13	— 8 14	Yes	Yes	Yes	Yes	No	No	No	do	No	Dry	do	do	Post-mortem decomposition				Colitis		Chronic colitis	
14	— 3 —	No	Yes	Yes	Yes	No	No	No	do	No			Right dilated and hypertrophied	do						Beriberi	
15	— 1 24	Yes	Yes	Yes				No	do	No	Moist	Ascites	do	Congestion, œdema	Normal	Congestion	Congestion	Normal		do	
16	— 1 10	No		Yes	Yes			No	do	No	do	do	do	Post-mortem decomposition						do	
17	— 2 25	Yes	Yes	Yes		No	No	Yes	do	No	Œdema	do	do	Congestion, œdema	Normal	Congestion	Congestion	Normal		do	
18	— 2 13	Yes	Yes	Yes		No	No	No	do	No	Moist	Moist	Normal	Œdema	do	do	do	do	Congestion	Undetermined[a]	
19	— 3 4	Yes	Yes	Yes		No	No	No	do	No	Firm	do	Right dilated and hypertrophied	Pneumonia	Congested	Albuminous degeneration	Albuminous degeneration	do		Lobar pneumonia	
20	2 5 —	Yes	Yes	Yes		No	No	No	Mixed	No	do	do	Normal	Congestion, bronchitis	Normal	Congestion	Congestion	do	Congestion	Acute tonsilitis bronchitis	
21	— 2 —	Yes	Yes	Yes		No	No	No	Breast	No	do	do	Right dilated and hypertrophied	do	Congestion	do	do	do		Beriberi	
22	— 1 21	Yes	Yes	Yes		No	No	No	do	No	do	Ascites	Normal	do	do	Nephritis	do	do		Nephritis	
23	— 2 18	Yes	Yes			No	No	No	Artificial	No	Œdema	do	Right dilated and hypertrophied	Congestion	do	Congestion	do	do	Congestion	Beriberi	
24	— 8 —	Yes	Yes	Yes		No	No	No	Breast	No	Firm	Moist	Normal	Pneumonia	Normal	Normal	Normal	do		Broncho-pneumonia	
25	— 2 —	Slight	Yes	Yes		No	No	Yes	do	No	Œdema	Ascites	Right dilated and hypertrophied	Congestion, œdema	Congestion	Congestion	do	do	Congestion œdema	Beriberi	
26	— 2 —	No	No	Yes	Yes	No	No	No	do	No	do	Moist	do	do	do	do	Congestion	do	Œdema	do	
27	— 4 —	Yes	Yes	Yes	Yes	No	Yes	No	do	No	Firm	do	Normal	Pneumonia	Normal	Albuminous degeneration	Albuminous degeneration	do		Broncho-pneumonia	

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[a] Greatly emaciated infant; death probably due to lack of assimilation of food.

Table X.—*Cases of alleged infantile beriberi.*

Case.	Clinical data ᵃ											Pathologic findings.											
	Age.			Berberic mother.	Feeding.	Convulsions or convulsive symptoms.	Fever	Urine.	Dyspnœa and cyanosis.	Vomiting.	Diarrhœa	External appearance of cholera.	Subcutaneous tissues	Peritoneum.	Heart.	Lungs	Spleen	Kidneys.	Liver	Intestines.	Meninges and brain.	Anatomic diagnosis	Bacteriologic diagnosis.
	y.	*m.*	*d.*																				
1	–	1	21	Yes	Breast	No	Yes	Scanty	Yes	No	No	Yes	Dry	Dry	Normal	Œdema	Congestion	Albuminous degeneration	Albuminous degeneration	Inflamed	Congestion	Cholera	Negative.
2	–	5	20	Yes	do	No	Yes	Diminished	Yes	No	No	No	Moist	Ascites	Right dilated and hypertrophied	Congestion	Normal	Congestion	do	Normal	do	Beriberi	Do
3	–	1	2	Yes	do	No	Yes	Anuria	Yes	No	No	No	Œdema	Moist	do	Congestion, œdema	Congestion	Albuminous degeneration	do	do	Normal	do	Do.
4	–	1	–	No	do	No			Yes	No	No	Yes	Dry	Dry	Normal	do	do	do	do	Inflamed	do	Cholera	Do
5	–	2	12	Yes	do	No	Slight		Yes	No	Soft yellow stools	No	Moist	Moist	Right dilated and hypertrophied	do	do	do	do	Normal	do	Beriberi	Do.
6	–	3	–	Yes	do	No		Suppressed	Yes	Yes	do	No	do	do	do	do	do	Congestion	do	do	do	do	No report.
7	–	3	–		do	No	Yes		Yes	Yes	Yellow	No	do	Ascites	do	do	do	do	do	do	do	do	Negative.
8	–	3	–	Yes	do	No	No		Yes	Yes	No	No	do	do	Normal	Broncho-pneumonia	Normal	Acute nephritis	do	do	do	Broncho-pneumonia	Do.
9	1	–	–	No	Artificial	No	No	Diminished	Yes	Yes	No	Yes	do	do	do	Congestion	do	Congestion	Congestion	Inflamed	Congestion	Enterocolitis	
10	–	3	–	Yes	Breast	No	No		Yes	Yes	No	No	do	do	do	Broncho-pneumonia	Congestion	do	Albuminous degeneration	Normal	do	Broncho-pneumonia	Negative.
11	–	5	–	No	do	No	No		Yes	Yes	No	No	do	Moist	Right dilated and hypertrophied	Congestion, œdema	do	Albuminous degeneration	do	do	do	Beriberi	Do.
12	–	1	17			No	No	Diminished	Yes	No	No	No	do	do	do	Congestion	Normal	Congestion	do	do	do	do	
13	–	2	–	Yes	Breast	No	No	do	Yes	No	No	No	do	do	do	Congestion, œdema	Congestion	do	Congestion	do	do	do	Negative.
14	–	1	–	Yes	do	No	No	do	Yes	No	No	No	do	Ascites	do	do	Normal	do	Albuminous degeneration	do	do	do	Do.
15	–	2	–	Yes	do	No	No	Suppressed	Yes	No	No	No	do	Moist	do	Congestion	do	Albuminous degeneration	do	do	Normal	do	Do.
16	–	1	25	Yes	do	No	No	Scanty	Yes	No	No	No	do	do	do	do	do	Congestion	do	do	do	do	
17	–	2	19	Yes	do	No	No	Anuria	Yes	No	No	No	do	do	do	Congestion, œdema	do	Albuminous degeneration	do	do	Œdema	do	Negative.
18	–	4	–	Yes	do	No	No		Yes	No	No	No	do	do	do	do	Congestion	Congestion	do	do	do	do	Do.
19	–	6	–	No clinical history obtainable								No	do	do	do	do	Normal	do	Congestion	do	Congestion, œdema	do	Do.
20	–	1	20			No	No	Diminished	Yes	No	No	No	do	Ascites	do	do	do	do	do	do	Normal	do	Do.
21	–	1	9	No	Breast	No	No	do	No	No	No	Yes	Post-mortem decomposition									Cholera (?)	Do.
22	–	1	21	Yes	do	No	No	Anuria	Yes	Yes	No	No	Moist	Moist	Right dilated and hypertrophied	do	Congestion	Congestion	Congestion	Normal	Congestion	Beriberi	Do.
23	–	2	–	No	do	No	No	Scanty	Slight	No	No	No	do	Ascites	do	do	do	do	do	do	do	do	Do.
24	–	1	3	Yes	do	No	No		do	No	No	No	do	do	do	do	Normal	do	do	do	do	do	No report.
25	–	1	17	Deaf mute	do	No	No	Anuria	do	No	No	No	do	do	do	Congestion, œdema	Congestion	do	do	do	Œdema	do	Negative.
26	–	1	19	Yes	do	No	Slight	Diminished	do	Yes	No	No	do	do	do	Congestion	do	do	do	do	do	do	Do.
27	–	1	27	Yes	do	No	No	Anuria	do	No	No	No	do	Moist	do	Congestion, œdema	Normal	do	do	do	do	do	
28	–	1	7	Yes	do	No	No		do	No	No	No	do	do	do	do	do	do	do	do	Normal	do	
29	–	3	–	No	do	No	No		do	No	No	No	do	do	do	do	do	Congestion, albuminous degeneration	do	do	Œdema	do	
30	–	5	–	Yes	do	No	No	Anuria	do	No	No	No	Œdema	Ascites	do	do	Congestion	Congestion	do	do	Normal	do	
31	–	2	5	Yes	do	No	No	do	do	No	No	No	do	do	do	do	do	do	do	do	Congestion	do	
32	–	1	13		do	No	No		do	No	No	No	do	Moist	do	do	do	do	do	do	do	do	
33	–	2	–	Yes	do	No	No		do	No	No	No	do	do	do	do	do	do	do	do	Congestion, œdema	do	
34	–	2	–	Yes	Mixed	Yes	No		Yes	Yes	Yes		Post-mortem decomposition									Undetermined¹	
35	–	2	23	Yes	Breast	No	No		Yes	Yes		No	Moist	Moist	Right dilated and hypertrophied	Congestion, œdema	Congestion	Congestion	Congestion	Normal		Beriberi	
36	–	2	–	Yes	do	No	No	Diminished	Yes			No	Œdema	Ascites	do	do	do	Congestion, albuminous degeneration	do	do		do	
37	–	1	20	Yes	do	No	No		Yes			No	Post-mortem decomposition									Undetermined¹	
38	–	1	6	Yes	do	No	No	Diminished	Yes	No	No	No	Moist	Ascites	Right dilated and hypertrophied	do	Normal	Congestion	Congestion	Normal		Beriberi	
39	–	1	10	Yes	do	Yes	No	Scanty	Yes	No	No	No	Œdema	Moist	do	do	Congestion	do	do	do		do	
40	–	8	–	Yes	do	No	No	Anuria	Yes	No	No		Post-mortem decomposition									do	
41	–	2	–	No	do	No	No	do	Yes	No	No	No	Œdema	Ascites	Right dilated and hypertrophied	Congestion, œdema	Congestion	Congestion, albuminous degeneration	Congestion	Normal	Congestion, œdema	do	
42	–	1	6	Yes	do	No	No	do	Yes	No	No	No	do	do	do	do	do	do	do	do		do	
43	–	2	10	Yes	do	No	No	do	Yes	No	No	No	do	do	do	Congestion	do	do	Normal	do	Œdema	do	
44	–	1	27		do	Yes	No		Yes	No	No	No	Moist	do	do	Congestion, œdema	Normal	Congestion	Congestion	do		do	
45	–	1	7		do	No	No	Diminished	Yes	No	No	No	do	Moist	do	do	Congestion	do	do	do		do	
46	–	2	20	Yes	do	No	No	do	Yes	No	No	No	Œdema	Ascites	do	do	do	do	do	do		do	
47	–	11	–	No	do	Yes	Yes		Yes	Yes	No	No	do	Moist	do	do	Normal	do	do	do		do	
48	–	1	20	No clinical history obtainable								No	Moist	do	do	do	Congestion	do	do	do		do	
49	–	4	18	Yes	Breast	No	Slight	Diminished	Yes	Yes		No	do	Ascites	do	Pneumonia	do	do	Congestion, albuminous degeneration	do	Œdema	Pneumonia	
50	–	1	22	Yes	do	No	No	do	Yes	No	No	No	do	do	do	Congestion, œdema	do	do	do	do	Congestion	Beriberi	

ᵃ In a great many cases the clinical observers noted changes in the voice, varying from weakness and hoarseness to complete aphonia.

¹ Post-mortem decomposition.

ILLUSTRATIONS.

PLATE I.

FIGS. 1–3. Hearts of infants dead of beriberi. The increase in size of the right ventricle is apparent.

FIG. 4. Heart of an infant dead of beriberi sectioned to show the large size of the right ventricle and the relatively small size of the left.

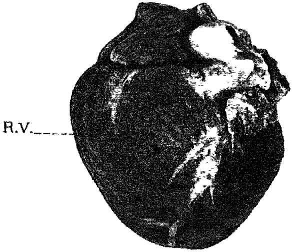


Fig. 1.

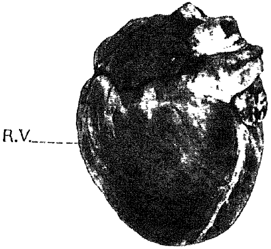
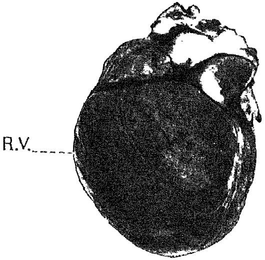


Fig. 2.



F.g. 3.

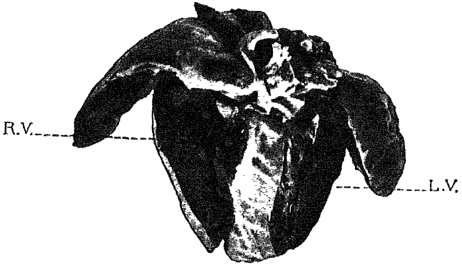


Fig. 4

PLATE I.

THE RELATIONSHIP OF FOOD TO PHYSICAL DEVELOPMENT.[1]

By D. McCay.[2]

"It is food that supplies the material for that perpetual series of transformations in which life consists, and it must be adequate in quantity and suitable in quality if these transformations, of so many different kinds, in so many different organs, are to proceed with that nicely balanced adjustment that is known as health."[3]

The question of the proper amount of daily food necessary to meet the physiological needs of the body is one that has occupied the attention of a great many workers since Chittenden stirred the nutritional pool. Believing that light would be thrown on the problem by a knowledge of the conditions that obtained in India, a series of investigations was undertaken to ascertain, if possible, the nutritive value of the different types of diet on which the teeming millions of India live. The inquiry soon resolved itself into one of determining the levels of nitrogenous metabolism attained on the different dietaries, and their effects on the physical development and well-being of the races investigated.

The dietaries being largely of a vegetable nature there is always an abundance of the carbohydrate element and a sufficiency of fat.

The first observations were made on students and others belonging to the Medical College, Calcutta, and also on some prisoners in the presidency jail. It was found that the average native of Lower Bengal on the ordinary diet of the province, namely, rice and *dal,* attains even a lower level of nitrogenous metabolism than Chittenden found to be quite compatible with health, bodily comfort, and the maintenance of strength and vigor. The observations made showed that students and members of the fairly well-to-do classes exist on a metabolism of less than 40 grams of protein per man daily. The great mass of the population is on an even lower scale than this. These results bore out Chittenden's views as regards the possibility of man existing on a protein content of the general diet less than one-third that of the ordinary standards, and, so far as they went, we freely admitted that the protein metabolism of the Bengali confirmed and corroborated his opinion.[4] It was when we tried to judge the effects of this dietary on the physical development of the race, the capacity of its individuals for manual labor, the condition of their blood and tissues, and, above all, their resisting power to disease and infection, that we were forced to part company from Chittenden and from the views he holds regarding the beneficial effects of a reduction of protein in the daily diet of mankind.

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[1] Read at the First Biennial Meeting of the Far Eastern Association of Tropical Medicine held at Manila March 14, 1910.

[2] Captain I. M. S., Professor of Physiology, Medical College of Bengal, Calcutta.

[3] Sir J. Crichton-Browne.

We showed the miserable standard of the Bengali's physical development, seemingly to be attributed to the low scale of protein absorption possible from their diet, by observations on students, prisoners, servants, and by an analysis of the records of the physical development of Bengali and Anglo-Indian students in the same college, under the same climatic conditions, doing the same work, but on a different diet. Without entering into any details of the work carried out on these lines, we may state that from the evidence brought forward, while admitting that it was quite possible for an individual or the members of a whole race to live on a metabolism of 6 grams of nitrogen daily, the results of this small intake on their general well-being, health, physical development, resistance to infection, and immunity from kidney disease[5] were not such as to confirm a belief in the sufficiency of Chittenden's standards. According to his views the metabolism of 0.12 gram of nitrogen per kilo of body weight is all that is necessary for the protein requirements of the body, which is practically the figure we obtained for the Bengali.

What are the effects on the physical development and general well-being of the people having this low level of nitrogenous interchange? The diet in Lower Bengal consists practically of rice and *dal* or pulse. It is an exceedingly bulky food when cooked, and, in order to provide for even the lowest limits of protein metabolism, a very large quantity has to be consumed; so large, as we have found, that the actual bulk interferes with its absorption.

The work on the Bengali showed, with regard to the chemical analysis of the blood, a higher percentage of water and a lower percentage of total solids and protein; the hæmoglobin was markedly reduced (about 75 per cent) and the blood pressure was on a distinctly lower level than that found among the Anglo-Indian students. We found that the results of these conditions were markedly to modify the physiological requirements of nutrition, and to a considerable extent to affect the growth and power of muscular contraction of the average individual, whose nitrogenous tissues are not given the option of drawing their nutritive material from so rich a source as more favored individuals do, nor have they the same opportunity of obtaining as free a supply of oxygen. We concluded from the study that the people on a diet from which only 37.5 grams of protein are absorbed live in a more or less chronic state of nitrogen starvation, leading to loss of body fat and tissue protein with an accompanying loss of vigor and strength and a comparatively low capacity for sustained muscular effort. From the evidence as to the physical development we came to the conclusion that the general physique of the Bengali is on a par with his diet, and that a close relationship exists between the poor physical development of this people and the meager protein absorption possible from the diet on which they subsist.

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[4] *Sci. Mem. Off. Med. & San. Dept.* Calcutta (1908), No. 34, 7, 8, 25, 28, 52.

[5] A point on which Chittenden lays great stress.

This was particularly well brought out by an analysis of the recorded weights, chest measurements, and heights of Bengali and Anglo-Indian students during the several years of attendance at one of the residential colleges in Calcutta. Under the same conditions but on different diets we found:

1. There was an increase of 7 kilos (14 pounds) in the average weight of Anglo-Indian and Eurasian students as compared with an average increase in body weight of 1 kilo (2 pounds) in the case of Bengali students on their diet, the observations being made over similar periods.

2. 42.8 per cent of the Bengali students showed a diminution in weight as compared with 2 per cent among the Anglo-Indian students. Among the former only 15.3 per cent gained weight continuously during the four years in residence, whereas practically all gained weight continuously among Anglo-Indian students.

3. The chest measurements bear out the same conclusions; the Bengali remains practically unaltered, whereas the Anglo-Indian increases his chest girth very considerably.

The diets on which these results were obtained are as follows:

Diet of Bengali students, in grams.		*Diet of Anglo-Indian students, in grams.*	
Protein (of which 9.3 were derived from an animal source)	67.11	Protein (of which 38.32 were derived from an animal source)	94.97
Carbohydrate	548.73	Carbohydrate	467.00
Fat	71.55	Fat	56.20

Comment on these results is unnecessary. They show very conclusively what may be expected in growing lads from diets respectively deficient and rich in absorbable protein.

Further evidence with regard to the physical endurance, capabilities of performing work, and the experiences of life insurance companies all place the Bengali on a low plane of physical development. The general consensus of medical opinion further shows that this power of resistance to disease is markedly inferior to that of the more highly fed European. Even in considering the incidence of renal disease, the facts do not bear out Chittenden's contention of the great advantage to the excretory organs of a low protein intake. Renal disease is much more common among the ordinary working population of Bengal and, in combination with diabetes, very much more so among the higher classes than among Europeans in Europe or India. This is all the more remarkable in a country where scarlet fever is unknown and where the consumption of alcohol by the people is almost negligible.

The general conclusion to be drawn from the investigations on the metabolism of the Bengali is that his physical development[6] is only such as could be expected from the miserable level of nitrogenous interchanges to which he attains.

From the results of work carried out on the Behari and other tribes of the plains of Bengal and United Provinces we obtained undoubted evidence of superiority in physique and muscular development and, what is also very noteworthy, a distinctly greater degree of vivacity, briskness, and sprightliness of manner. The body weight is also on a higher scale, being on the average 5 to 7.5 kilos greater than is the case with the Bengali. The ordinary working population of Bengal is characterized by a want of vigor, a slackness, tonelessness, general slowness of reaction, and other physiological attributes of torpor difficult to describe, detect, and measure. Self-absorption and want of interest in the incidents of everyday life, little power of attention, observation, or concentration of thought are some of the attributes of all but the better classes and of the better fed among the Bengalis. The Behari and the inhabitants of United Provinces do not show these characteristics to anything like the same extent. What kind of dietary do these people live on? The Behari lives on a mixed diet of wheat, maize, rice, and *dal;* the inhabitants of Agra and Oude live largely on wheat, different millets, barley, maize, and *dal.* Without going into details of the different foodstuffs it may be accepted that the ordinary workingman has a diet from which he can absorb at least 9 grams of nitrogen per day. Rice as a rule forms no part of the dietary. This would give a metabolism for the different races included above of from 0.15 to 0.18 gram of nitrogen per man daily, a quantity that Chittenden would consider excessive, and it is fully 20 to 50 per cent superior in its most important element, nitrogen, to the dietaries of Lower Bengal. As we have already stated, the physical fitness and development of these races are much superior to the same characters obtaining in Bengal, and, as far as the evidence goes, the latter would appear to obey the biologic law, namely, their protoplasmic development is a function of the absorbable protein of the diet.

Now the question arises, Are there any other factors except differences in diet that will satisfactorily account for this higher standard of physical development and general well-being?

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[6] The actual amount of protoplasmic tissues as distinguished from fatty tissue.

We believe the presence of wheat, maize, millets, etc., replacing the bulky rice, which is of low nutritive value, sufficiently explains the situation; however, we shall examine some of the objections which have been brought forward against the view that defective nutrition is the result of a low protein intake.

Doctor Kellogg, a strong advocate of vegetarianism, criticised our finding regarding the important rôle played by diet, and especially by protein, in the nutrition of the Bengali, as follows:

> The weakest part of the report from my standpoint is the remarks which the investigator makes in relation to the defective nutrition resulting from the low protein dietary. I do not think it is at all fair to attribute the lack of endurance often seen among Indians to the low protein diet. There are so many factors which certainly should be taken into consideration. Among these are their sexual excesses, the depressing effects of the very hot, damp climate in which they live, and which predispose to lack of exercise, the injurious effects of excessive, prolonged exposure to the actinic rays of the sun. Still another factor of importance is the immature age at which these people usually marry. Many of the Indians, however, are strong and robust people. I understand that an Indian regiment made up entirely of natives is the finest lot of men in His Majesty's service.

We agree that these causes have undoubtedly an influence in retarding growth and lowering the general standard of physique, and, if there were no means of estimating their effects, it would be very difficult to say that they are not quite sufficient, as Doctor Kellogg believes, to account for the relative difference between Europeans and the poorer developed natives of India.

Many objections to Doctor Kellogg's views immediately arise, for instance, as regards climate and the actinic rays of the sun. Europeans, Eurasians, and the better-fed Bengalis are all equally exposed to these influences, yet retain their energy. We have made inquiries regarding sexual excess, and, while masturbation probably is more prevalent among the Bengalis, excessive sexual congress is chiefly practiced by the better classes, who have the means and energy to satisfy their desires. Immature marriage is undoubtedly a factor, but there are customs which have a tendency to neutralize its ill effects: The husband and wife do not live together until the wife reaches puberty—the husband is usually several years older than the wife, and the latter spends about one-third of each year with relatives away from the husband. Another effort of nature to maintain the standard is the relatively higher death rate amongst the children born early in marriage. However, while these replies to Doctor Kellogg's criticisms are important in showing that his objections do not cover the whole ground, it is evident they are too indefinite to be measured and appraised at their full value. They would, even at the best, be only a matter of opinion, one school of thought looking on them from a point of view different from that of another.

In order to obtain definite and precise knowledge as to the effects of diet *per se,* we have extended our inquiries to different tribes and races in which the several factors enumerated by Doctor Kellogg are common to all, the dietaries forming the main point of difference. In this way we can eliminate the influence of the sun's rays, early marriages, climate, sexual excess, etc., in fact everything except the rôle played by diet, or, more particularly, absorbable protein, in the conditions that go to make one class superior to another, or one tribe or race superior to another tribe or race.

We find the different tribes and races whose characteristics we have been discussing inhabiting the plains extending from the sea opposite Bengal to the base of the mountains bordering Bengal, the United Provinces and the Punjab on the north. Now, all the factors Doctor Kellogg laid stress on are present amongst these people. The climate from Behar to the mountins, north and northwest, is to all intents and purposes the same; early marriages, sexual excesses, actinic rays of the sun, etc., are all even more in evidence than in Bengal; yet when we come to investigate the different attributes that go to make up a man, we find that there is an ascending scale of physique and manly qualities among the inhabitants extending from Lower Bengal to Behar and from Behar to the Provinces of Agar and Oude. There is an ascending scale of body weight and particularly of the protoplasmic tissues. A decided change in the demeanor and general appearance takes place as we pass from plain to plain, the people becoming brighter, fitter, and more energetic in their movements,

It may therefore be concluded that diet appears to play the principal part in the formation of the respective characteristics and general bearing of these races. The difference in diet is the substitution of an assimilable form of protein in the shape of nonbulky foodstuffs for a bulky material (rice) of low nutrition value, or, translated into its ultimate effects, the metabolism of 9 grams of nitrogen instead of 6 grams as found in Bengal.

With regard to the last part of Doctor Kellogg's criticism we may say a few words.[7]

It could not be expected that a person who had never been in India would be in a position to differentiate between the races; so that the inclusion of the Bengali among the great fighting races is, therefore, quite easily understood; nor would the point call for any comment were it not that true facts afford still further evidence of the important rôle played by diet. The Bengali has never, in modern times, so far as we are aware, been recruited for the fighting line, and although many regiments are, or were, called Bengal infantry, Bengal cavalry, etc., not a single man carrying a rifle could claim Lower Bengal as his place of birth. We have no desire to elaborate the point, but the question arises, Why is the Bengali unfit for the fighting line when other inhabitants of the plains exposed to, and suffering from, all the disabilities that Doctor Kellogg enumerates, but living on a superior diet, are capable of exhibiting the firmest courage and of maintaining untarnished the great fighting traditions of their race? Thus we have the Sikhs, famous throughout the world for their endurance and fighting qualities, inhabitants of the hottest plains of India, yet men of splendid physique and full of energy; the Dogras, Jats, Rajputs, all well known for their own special qualities on the Indian frontier, or wherever courage, endurance and determination are called for. These races labor under the disadvantages advanced by Doctor Kellogg to explain the relatively poor development and lack of endurance of the Bengali, but we have obtained no evidence from a study of these people of the correctness of his opinions.

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[7] "I understand that an Indian regiment made up entirely of natives is the finest lot of people in His Majesty's service."

Even in the various classes of these and allied races differences in physique, muscular development, hardiness and all those qualities that go to make up the perfect soldier can be detected. We believe that diet, and particularly the level of nitrogenous metabolism attained, has an immense influence on the formation of those most desirable characteristics of the races whence is drawn our best fighting material.

We have made extensive inquiries on the same lines among the hill tribes of Bengal and have no hesitation in asserting that the evidence obtained confirms and corroborates the view put forward as to the rôle of assimilable protein and its determining influence on the physical development and character formation of a people. We took up the different tribes inhabiting the hills around Darjeeling and contrasted, as far as possible, the physique and general characteristics of the several races. While there is no doubt but that climate has a great deal to do with the higher scale of general development and capabilities of these tribes as compared with those of the plains, this is not the whole story as is brought out by a comparison of the several classes living under practically identical conditions, but with a difference in diet forming the one conspicuous influence on their respective attributes.

We do not wish at present to go into details of the work carried out on these hill tribes. Suffice it to say that the Bhutia, by far the most capable of these people in those occupations requiring great muscular exertion, attain a nitrogenous metabolism much higher than that of any other tribe, or, indeed, any other race we have investigated. Just as was the case with the inhabitants of the plains, so we find with the races in the hills that variations in the level of nitrogenous metabolism appear to be the determining factor of the several causes that go to relegate, fix, and maintain the position of a tribe or race in the scale of mankind.

The close relationship between the nutritive value of the several dietaries and its influence on the physical development of the different tribes and races that we have investigated is clearly brought out in the following scale of the degree of nitrogenous interchanges:

	Grams of nitrogen per kilo body weight.
First. Bhutias	
Nepalese Bhutias	[8] 0.42
Tibetan and Bhotan	[8] 0.35
Sikkim Bhutias	0.25
Second. Nepalese	0.18–0.25
Third. Behari	0.15
Fourth. Bengali and Ooriya	0.116

We have only taken into account the inhabitants of Bengal, as the work in other provinces is not yet completed; but nothing we have learned in further investigations has tended to contravert the opinion we have expressed; on the contrary, the more the subject has been gone into the stronger the evidence becomes of the correctness of our views. Every possible cause, *except diet,* has been put forward as offering a complete explanation of the inferior capabilities of the Bengali as compared with those of the great races of the plains of India. We have discussed these hazy, ill-defined influences, and, while admitting the probable force of some of them, have eliminated them by contrasting races in which all the factors are identical, but in which diet alone forms the distinguishing element, or, more correctly, in which the level of protein metabolism forms the great line of demarcation. We conclude from the studies that absorbable protein is the all-important element in the physical development and general well-being of mankind.

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[8] Diet very highly animal.

UNSOLVED HEALTH PROBLEMS PECULIAR TO THE PHILIPPINES.[1]

By VICTOR G. HEISER.[2]

Many of the modern problems of hygiene and sanitation are the same the world over, whether found in tropical or temperate zones. There are certain characteristic phases of tropical hygiene and sanitation, however, which have received most gratifying attention in recent medical literature and which we can not but interpret as showing a very general interest and desire to make these portions of the world compare in healthfulness with those heretofore believed to be more favorably situated. However, in addition to these general problems, common to all tropical countries, there are additional difficulties and handicaps peculiar to each country or people, which have required special consideration.

It is the object of this paper not only to present the problems and theories with which you are already familiar, for it is desirable that you should know what we also are doing along these lines, but more especially to put before you the peculiar conditions which have seemed to hinder our more rapid progress and which are still blocking the way to better sanitation and hygiene in the Philippine Islands.

In general, we have first a poverty-stricken people with a poor physical inheritance, a people strongly imbued with superstitions and habits the antithesis of the simplest health doctrines and practices, a people lacking ambition productively to till the fertile soil, a people the masses of whom are apparently content in their ignorance and poverty and resigned to and uncomplaining of their many ailments. Work among them is handicapped by the inaccessibility of many of the islands and the nature of the roads, which, although being improved at a remarkable rate, are yet unfit for travel in many instances during portions of the year. It is further handicapped by the lack of a common language, for as many as fifty or more dialects are spoken among the *tao* or peasant classes, to whom neither Spanish nor English is intelligible. It is handicapped by the lack of a sufficient number of medical employees who are sufficiently interested in the cause of humanity to undergo the innumerable hardships and discomforts which accompany most of the medical service in the provinces. Untold credit is due those who are at present carrying on the work, the burdens of which fall more heavily upon them because of their limited numbers. We are also handicapped by a treasury of which it is quite possible at times to see the bottom, so that it is not put to us, "do all you can regardless of expenditure," but "your expenditures must not go beyond this or this; do the best you can with the funds available." So our very largest problem is that of discrimination: Shall we devote our energies to this or that question; we cannot do all; shall we attempt this one and abandon that, or do a little toward each? Thus far it has been our policy to do a little toward each, although the problems are many and great.

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[1] Read at the first meeting of the Far Eastern Association of Tropical Medicine, held at Baguio, P. I., March 14, 1910.

[2] Passed assistant surgeon, United States Public Health and Marine-Hospital Service; Director of Health for the Philippine Islands; and Professor of Hygiene, Philippine Medical School.

Malaria.—For instance, the malaria problem alone is a very large one. In the Province of Ambos Camarines, which has a population of 233,472 persons, there were 745 deaths from this disease reported for the year ended June 30, 1909. A conservative estimate of 10 cases for each death with an illness of ten days makes 74,500 days lost, which, valued at only 50 centavos Philippine currency or 25 cents United States currency a day, would amount to 37,250 pesos or 18,625 dollars United States currency a year. This being for only 1 out of 30 provinces, we can conservatively multiply this sum by 20, which would make an economic loss to the country of 745,000 pesos. If a human life can be economically valued at 1,000 pesos or $500 or £100 in this country, making deductions for children, etc., we find ourselves confronting a loss of at least 5,000,000 pesos per annum from this disease alone, and yet this represents but a small portion of the total loss which can be attributed to preventable diseases.

The number of malarial cases has been greatly decreased, however, by instituting drainage wherever possible, by the free distribution of quinine, and by campaigns of education, particularly in the schools, where pupils are taught the value of mosquito nets, the danger from mosquitoes, and how they may be destroyed, etc.

Mosquitoes.—There recently has been an active newspaper agitation concerning the eradication of mosquitoes in Manila, but few persons realize the obstacles that block our way in such an undertaking. Manila is on low land, much of its area being in fact below sea level. To bring the city to a drainable level would be a necessity in such a proposition, and is estimated to cost 4,000,000 pesos at least. When we reflect that the annual income of the city is under 3,000,000 pesos we naturally pause before recommending a measure so financially disproportionate, especially when some authorities consider such an undertaking problematical and more especially since there are practically no reliable data on hand to show that the mosquitoes of Manila are more serious than a physical annoyance. We can well imagine how a similar proposition would be received in the United States or any other country. Should we expect it of these Islands, overburdened as they are with more acute problems? It seems to the writer more logical to begin mosquito elimination in Manila, at least, by educating the individual householder to make the breeding of mosquitoes on his premises impossible, and then by an organized inspection service to enforce regulations which will compel the use of such knowledge. In the meantime, a definite engineering project should be adopted and carried out in a limited way. Drainage and filling and oiling might be tried with the regular sanitary corps as far as possible.

Water supply.—The water supply of the Philippine Islands is another serious question. All surface waters found in the Islands except the thermal waters, or those strongly charged with certain minerals, are infected with amœbæ. Improved health conditions in Manila can to a certain extent be traced to the new city water supply which now comes from a comparatively uninhabited watershed, but even as tap water it should be boiled for all but the most ordinary purposes. Fortunately, artesian-well water is as a rule free from amœbæ, and is in every way an ideal drinking water. In towns where artesian well-water is almost exclusively used the death rate has fallen 50 per cent. These wells are being drilled as rapidly as possible, but there are many localities where they are impracticable, so that the question of how to make available for the people an unlimited and safe water supply, exclusive of artesian-well water, must be considered one of our unsolved problems.

Disposal of excreta.—We are still pondering the practical disposal of excreta. Many plans have been proposed, all more theoretical than practical. Of those who are familiar with local conditions and who realize the resources and limitations of the average community, but who are seriously searching for a practical solution, none as yet has put forth a well-defined scheme.

In large communities where water carriage of sewage is possible septic tanks are used successfully. In communities in which cholera has prevailed the pail system, the digging of pits and covering of excreta with lime or clean earth at regular intervals, has been found effective, but the cost of maintenance and inspection as a regular measure is prohibitive and only warranted by emergency conditions.

Some years ago the writer suggested a plan of installing a pail system with an after treatment of the night soil which would render it suitable for fertilizing mulberry trees, thus promoting the silk industry, the income from which would in a short time place this particular sanitary measure upon a self-paying basis.

The plan followed in many oriental countries of letting out private contracts for the collection of night soil from private residences is not believed to be a safe one. It is an established custom to use such night soil for fertilizing vegetables, and it is believed that the consumption of raw vegetables thus fertilized has had much to do with the spread of amœbic dysentery, cholera, hookworm, and other intestinal diseases.

Smallpox.—Smallpox, once so formidable a proposition to us, has at least been reduced to insignificant proportions. Over 6,000,000 persons have been vaccinated by the Bureau of Health within the past five years. The unvaccinated are in remote regions where as yet it has been found impossible to convey vaccine in a potent condition.

The ordinary glycerinized lymph at present in use will not keep for more than seven to ten days at the temperature which prevails here. As many of the sections to be reached are in traveling time from two to three weeks away from the point to which ice can be sent, or where cold storage is available, it is obvious that a vaccine is necessary which will retain its potency for a longer period of time than any now obtainable. Vaccine in powdered form has been tried, also dry points, but the percentage of success is so small and danger of infection so great that their use is restricted.

The acute phase of this problem then is either to manufacture a more effective vaccine or to find a way of transporting it successfully. Observations point to the conclusion that ordinary cowpox vaccine is not as effective among the dark as among the white skinned races. The writer has personally observed that out of more than 100 cases of smallpox or varioloid among white people not one case occurred in a person who had been vaccinated within five preceding years, while there have been many cases of smallpox among Filipinos of whose successful vaccinations within one preceding year there could be little doubt.

It has been interesting to observe a demonstration of this at Bilibid Prison, where all prisoners are vaccinated upon admittance, and regularly once a year or oftener thereafter. Yet smallpox has made its appearance there each year, and many cases have occurred in persons who show the typical pits accepted as characteristic of previous attacks of smallpox.

Tuberculosis.—Tuberculosis is another of our problems. We estimate that it claims as many victims as in other portions of the globe, and it will require the same activity here as elsewhere to hold it in check. The introduction of out-patient tuberculosis dispensaries, the construction of shacks in the mountains, the opening of night camps near Manila, arrangement for the hospitalization of the helpless sick and prophylactic instruction in the public school, the usual methods in fact that are employed elsewhere, are now under way here; but the tuberculosis problem has its peculiar and complicating features in the Philippines, namely, the unsuitable dietary of the people, their peculiar superstitions concerning the contraction of the disease, their almost unshakable fear of night air as a poisonous thing, a fear which has kept their houses tightly closed at night for generations past, their habit of chewing betel nut which has made the custom of expectorating in public and private a universal and we sometimes fear an incurable habit. Added to this is their utter resignation to the disease as a thing incurable and inevitable. Therefore, not only have we the ordinary preventive and curative measures against tuberculosis to organize and enforce, but we must devise ways of cooking and preparing native products into a suitably nourishing and popular dietary, and then educate the masses not only to the ways of adopting these reforms, but also to an earnest desire for them. They will have to be first cured of their superstitions, which is as great a task as converting them to a new religion; houses will have to be opened at night, betel nut chewing gradually abolished, and then a gigantic antispitting crusade begun, and, last of all, comes the Herculean task of rousing them out of their inertia and convincing them that not only is tuberculosis curable, but that they are responsible for the spread of the disease and able to themselves accomplish the cure.

Cholera.—Cholera is still with us in spite of the active measures which are constantly being taken to eradicate it. Although we have so far been successful in promptly suppressing outbreaks whenever they appear, yet it is constantly occurring in sporadic form over widely separated sections of the Islands. The puzzling question is this: When no possible connection with any previous case is discoverable, where are the cases of cholera contracted that appear so spasmodically over these widely separated regions? Whether it is lying dormant during the periods of time when no cases are reported is yet to be determined. Some years ago the writer drew attention to the fact that logical deduction indicated that there was a morphological change in the cholera organism which made it difficult to recognize at certain stages. Research work done in the meantime strengthens this view. There is also a strong probability that cholera carriers are responsible for some outbreaks; yet the fact remains that the disease appears frequently at places in which its origin can not satisfactorily be proved.

Plague.—Plague at present is a stranger to the Philippines. Measures for its eradication were begun in 1900, but it was not until the heretofore-described scheme of dealing with rats was used that the disease disappeared. Since April, 1906, no cases have been found in human beings, and no cases in rats since 1907.

However, on account of the close proximity of China, where plague seems to appear every year, special precautions are constantly taken at our ports in order to prevent the reintroduction of this disease. The question of course is how safely to accomplish this with a minimum amount of annoyance and loss to the shipping interests and to the traveling public. The present plan is to fumigate all vessels from infected ports twice annually and to keep the interisland vessels free from rats and vermin by systematic fumigation, in order that the plague may at once be checked if by any accident introduced. Wharves have been made rat proof, and vessels where docked are required to use rat funnels in order to keep rodents from gaining access to the shore. At the port of departure for these Islands vessels are inspected by medical officers of the United States in order to ascertain that there is no plague aboard.

Typhoid fever.—While cases of typhoid fever are undoubtedly contracted in the Philippines, yet the disease can hardly be said to be prevalent here. To prevent its establishing a foothold, regulations were prepared for the disinfection of excreta from such cases, for the protection of water supplies, and regulations concerning inspection and sale of milk; also sanitary measures for the eradication of flies were undertaken. Whether further and more stringent precautions could be taken at this time, or are practicable, is a question for consideration.

Infant mortality.—The subject of infant mortality is a vast one. In Manila approximately one-half the total number of deaths occurs in children under one year of age. From papers read at this meeting and previously it is obvious that the largest share of it is due to improper nourishment. The poverty of the people makes properly marketed cow's milk, either fresh or canned, an impossibility unless given in the form of charity. This for the great mass of people is not only impossible but undesirable. How to bring a cheap supply within the reach of the poorer classes seems to be the acute phase of the infant-mortality problem. The raising of goats would seem to be the solution. Already experiments in breeding a hardy variety of milk goats have been inaugurated. This problem must not be abandoned, but be rapidly pushed to a solution; for if left unsolved it involves the heaviest mortality we are at present facing.

Putrefactive changes in foods.—Another complicating feature and cause of illness in the Tropics, particularly in the Philippines, is the putrefactive changes in nitrogenous foods which take place so rapidly in warm climates. The problem is either to provide ways properly to preserve such foods or to find suitable substitutes which will enable us to eliminate them from our tropical dietary.

Insanitary habits.—The food question brings in its trail another problem that is peculiarly ours and which we know to be the largest factor in the transmission of cholera and intestinal diseases. This is the habit of eating with the fingers. Proper example has done much and the distribution of literature on the subject has helped; but the masses are as yet untouched by either example or precept, and we see years of discouraging struggle ahead of us before they can be broken of so fixed a habit, the menace of which is as yet entirely beyond their comprehension.

Poor statistical information.—So much for the particular problems.

The entire situation is hindered by our inability to secure proper statistical information. This is due to a lack of officials in the provinces sufficiently skilled to make reliable reports on the causes of death. Whether the municipal officials can be trained and educated to do this remains to be seen. As stated in the beginning, our work is first one of discrimination, a placing of our heaviest artillery where the enemy is strongest. This we can not always determine on account of the inaccuracy and incompleteness of available data.

SUMMARY.

To summarize, it is to be understood that the health of these people is the vital question of the Islands. To transform them from the weak and feeble race we have found them into the strong, healthy, and enduring people that they yet may become is to lay the foundations for the successful future of the country. But it is not alone the problem of the Bureau of Health; it is an economic and educational question as well. Every branch of the Government has its part to perform, and coöperation is essential. Good roads: agricultural improvements; the elimination of rinderpest and other animal diseases; the general development of the country, which will gradually bring about a better standard of living; education, particularly along the lines of hygiene and sanitation (to which we give all the aid possible, but for the dissemination of which we will have to depend upon the teachers and the public schools); the special training of the young men and women of the Islands in the professions of medicine and nursing—all the foregoing factors, with which we, as a Bureau, have nothing to do, are as important to the health conditions of the Islands as is the actual holding in check of epidemics and disease, the sanitary inspections, enforcement of regulations, etc., the opening and maintenance of hospitals throughout the Islands, and the various other things for which the Bureau of Health is directly responsible.

The Government is not a rich one. How to do the most and the best with a limited income is still an acute question. You can see what an enormous proportion of that limited income it would take to carry out successfully any one of the various health projects enumerated. To give thorough attention to a particular one would involve an unwarranted neglect of the rest. Hence we have concluded we must do the best we can with the entire proposition, going slowly but making headway each year, each month, perhaps each day.

It should be remembered that much of our appropriation is consumed in ways unusual for a health bureau. The maintenance and management of general and insane hospitals, orphan asylums, homes for the aged, etc., falls to our lot and is no small burden. We are practically cleaning up these Islands, left foul and insanitary and diseased by generations of hygienically ignorant peoples. We are stamping out the conflagration of disease started long before American occupation, and not until it is stamped out can we look forward to the modern problems which come so temptingly before us. And so, much of our time, money, and effort is being constantly consumed in works, the glory of which is still behind the clouds. We are draining the land, as it were, before beginning the constructive health projects which are going to make these people the strong and healthy race we intend them to be.

THE PARTHENOGENESIS OF THE FEMALE CRESCENT BODY.

By H. M. Neeb.[2]

As is well known, the parthenogenesis of the tertian gamete was first observed by Schaudinn in a patient, Mrs. Kossel, and was accurately described by him. This discovery is very important as it gives a clear and natural explanation of the cause of relapses in malaria, particularly in persons who have long since left the Tropics and are no longer exposed to active infection. This observation of Schaudinn was afterwards confirmed by Doctor Von Hilst Karrewly and then by Doctors Merz and Blüml.

It seemed highly probable that a metamorphosis of the tropical and quartan parasites would occur in a similar manner and should be sought for in a similar way. When I was in charge of the civil medical service at Koeta-Radja, during the hours of free consultation, I often had the opportunity of preparing blood-smears from natives who had contracted fever and had never been treated with quinine. Many of these patients were suffering from a severe infection with tropical malarial fever. For a long time my investigations were fruitless. However, two and a half years ago I examined blood-smears from a Bengalese and discovered the particular forms of parasites shown in Plate I, figs. 1, 2, and 3.

After an exhaustive consideration of every conceivable hypothesis, I finally came to the conclusion that I probably had encountered parthenogenesis in the female tropical gamete. However, I hesitated to publish such a discovery without accurate verification and confirmation by competent authorities on malaria; therefore, I took the opportunity, during my furlough, to have my slides examined in Europe at Bordeaux and Hamburg.

In the former city, Professor Le Dantec declared the forms represented by figs. 1 and 2 to be sporulation parasites, but quite different from those which are found in the common schizogenesis of the tropical parasites. However, he went no further than to state that in every case they were derived from a gamete.

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[1] Read at the first meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 10, 1910.

[2] Medical officer of the first class, delegate from Her Majesty's Government of the Netherlands Indies.

The experienced protozoölogist, Doctor Von Prowazek, of the "Institut für Schiffs and Tropenhygiene" at Hamburg, declared the forms shown in figs. 1 and 2 to be parthenogenetic ones of the female crescent bodies. Professor Nocht found figs. 1 and 2 to be very interesting. He had never seen such forms, and, after due consideration, agreed with me that we are dealing with a case of parthenogenesis. Both the temporary assistant, Doctor Rodenwaldt, of the army, and Doctor Gonder, assistant to Doctor Von Prowazek, suggested it to be barely possible that the forms represented two microgametocytes, in which the chromatic mass had just divided to produce the microgametes, which would have been expelled forthwith. I believe I can bring forward a number of well-founded objections to this view, as will be seen from the discussion below. Doctor Werner was of the opinion that an exact critique was scarcely possible, because the blood-smears had been stained with Giemsa solution to which a small quantity of a solution of potassium carbonate had been added, and under such circumstances it was not inconceivable that other portions of the cell and of the parasite might also have been stained in the same manner as the chromatic substances. Doctor Mayer also found the forms under discussion to be very peculiar, but hesitated to express a definite opinion regarding them.

The interpretation of the parasitic forms which I demonstrated was still difficult, even after such authorities on malaria as Le Dantec, Nocht, Von Prowazek and others had examined the slides. I therefore determined, to the best of my ability, further to elucidate this point by preparing colored plates of the segmenting parasites, accompanied by a detailed description of the latter. The facts regarding the preparation of the specimens are as follows:

To the best of my recollection the Bengalese patient already mentioned came to me during my consultation hour. He appeared to be very feeble, was anæmic and cachectic. His temperature was between 38° and 39°C. The liver and spleen were enlarged. He had never taken quinine.

I prepared two slides in the usual way from a drop of blood. The blood on the slides was congealed in a few seconds by rapidly swinging them; then the preparations were immediately fixed with methyl-alcohol and afterwards stained for two hours with Giemsa solution (Grubler, Leipzig), 1 to 20, mixed with two or three drops of potassium carbonate, 1 to 1,000.

Beautiful examples of Maurer's *"perniciosa granules"* could immediately be observed on the infected red blood corpuscles. The corpuscles themselves were not enlarged and they had the usual red color. One or occasionally two tropical rings were generally to be found in the infected chromocytes and these were as a rule grown. However, the majority showed the peculiarity of containing one very large and, in certain instances, a double chromatic mass, the protoplasmic ring being proportionately very broad and coarse. I believe that many of these forms should be considered as young gametes, which later would have become crescent bodies.

Moreover, many crescent bodies could be found, for the most part female, which were almost full grown, or had recently attained maturity and which were still inclosed, more or less, in membranes of different form and of a dark, brick color. The envelope was very distinctly recognizable as the stroma of the chromocyte. In addition, a slight polychromatophilia was present; basophilia could not be observed. However, there were peculiar, very large, retiform, brick-colored cells (macrophages from the spleen) and also a few macrocytes.

After careful and repeated examination of the blood preparations, I arrived at the conclusion that a mixed infection was certainly not present, because only large rings of the tropical parasites, situated in chromocytes showing Maurer's spots and crescent bodies, could be found.

In addition to the blood constituents already described, the forms shown in figs. 1, 2, and 3 were seen in the slides. These were examined with a Zeiss oil-immersion one-twelfth objective and No. 4 ocular, giving a magnification of 950. However, as an exact representation of all the details presented many difficulties when such an enlargement was used, I sketched figs. 1, 2, and 3 on a scale about 1.5 times greater, and they thus possibly represent an enlargement of 1,500; on the other hand, figs. 4 and 5 are magnified only 950 times. If, now, we examine figs. 1 and 2, it becomes evident that the parasitic body occupies almost all of the red blood corpuscle, which is neither enlarged nor faded. In fig. 3 it occupies approximately two-thirds of it; figs. 2 and 3 show some large parasites and fig. 1 two which are very minute. An elongated oval form may be seen in fig. 1. This is indented on the right margin and has an obtuse and slightly deflected point at the right upper corner, this point being quite similar to that of many young crescent bodies in the same blood slide. On the other hand, the opposite pole of these young gametes is either round or obtuse. In fig. 2 the parasite is oval, with the narrower pole directed downwards, whereas that of fig. 3 resembles a crescent body with a convex projection on the concave side. The protoplasm of the malarial parasite is stained a very light violet-blue in figs. 1, 2, and 3; in figs. 1 and 2 blue predominates; in fig. 3, violet-red, and this color of the protoplasm corresponds exactly to that of the crescent bodies in the blood slides. We find in this protoplasm in fig. 1, especially at the left-hand upper corner parallel to the contour of the parasite, but not touching the periphery, a distinct, band-like, light violet-red chromatic mass of basic material in which may be observed small, dark red-brown, chromatic bands which are generally situated at right angles to the former. In these small bands may be seen one or two chromosomes (nuclear masses) stained very dark purple. This light, red-violet basic substance is probably to be looked upon as a metamorphic change between the proper chromatic material and the protoplasm of the parasite. Between this broad, band-like basic mass and the periphery of the parasite we see imbedded in fig. 1 small, detached, chromatic points. In fig. 2 the light red-violet, band-like basic substance runs parallel to the periphery of the parasite, but touches the circumference almost at every point and incloses three-fourths of the contour of the parasite. In the right, lower quarter there is an isolated islet of the same substance in which are imbedded two large, detached chromosomes.

Whereas we detect about 15 chromatic nuclear dots in fig. 1, in fig. 2 we find only about 12 of them. In fig. 3, where both poles and the remainder of the parasite show very distinctly that it is derived from a crescent body, the chromatic band may easily be distinguished as a crescent which runs from the upper left- to the lower right-hand corner of the parasitic body in such a manner that the greater part of the convex margin of this band does not touch its concave inner side. A protoplasmic zone, which in some places is very narrow, may be seen intact between the two margins. In the basic mass of this band we find imbedded darker chromatic dots. In the upper half these are very rare, are small and not very distinctly differentiated; in the lower half they are much more distinct and are more or less detached, resembling particles of the basic material. Indeed, two of these spots lie in the contiguous protoplasmic substance of the parasite. Furthermore, we find in fig. 1 an indefinite mass in the lower left-hand segment, consisting of irregularly scattered, varicolored, small chromatic dots, with transparent spots situated between them, making it appear as though the parasite were perforated by pinpricks. Between these, and also in the upper right-hand portion, a very typical, yellow-brown, coarse pigment occurs which bears all the peculiarities of the pigment of the crescent bodies. This spot, which is not easily defined, may, after the analogy of the tertian macrogamete, be considered as an unfertilized body (*Restkörper*), in course of decomposition. Two large perforations may clearly be seen in fig. 2, and one smaller one, somewhat beyond the actual center of the parasite. Around these perforations the beautiful, yellow-brown pigment of the crescent body is visible. However, a distinct unfertilized body (*Restkörper*) can not be discovered.

In fig. 3 the corresponding pigment lies in the center of the protoplasm. Here it is very beautifully imbedded and arranged like the stamens of the calix of a flower.

We may affirm, without fear of contradiction, from the morphological characteristics already described, that in figs. 1 and 2 we are dealing with segmenting forms. I wish by the following argument to meet the objection raised by Doctor Rodenwaldt that, after all, these might be microgametocytes, the chromatic substance of which is in the act of disintegration, the microgametes being about to be expelled.

1. As far as I know, microgametocytes, of which the chromatic substance had already been segmented for the microgametes which are to

be expelled, have never been seen in instantaneously congealed blood slides containing tropical gametes. A segmentation of the chromatic substance which has progressed as far as it is shown in figs. 1 and 2 would also, in my opinion, be impossible during the few seconds occupied by the process of congealing, unless we were inclined to concede that the segmentation had already begun in the circulating blood, which, however, has not up to the present time been proved. We can only continuously observe and follow the expulsion of the microgametes in fresh. uncongealed blood containing male gametes for fifteen to thirty minutes after its withdrawal from the body.

2. The chromatic particles, if they were destined for the microgametes which are about to be expelled, would greatly surpass the latter in number. In fig. 1 we have approximately 15 of these and in fig. 2 about 12. As far as I know, such a large number of microgametes is never formed by one microgametocyte.

3. The parasitic forms sketched in figs. 1 and 2 are much too large for tropical microgametocytes. Moreover, the form of this intracellular parasite is not in accord with such an hypothesis. It follows that we have to do with a sporular form. Therefore, we have only to decide, first, whether it is a case of a sexual segmentation or one of parthenogenesis of a macrogamete, and, second, the species of the parasite.

Forms of malarial parasites of other mammals and birds may be immediately excluded from consideration, because it has been proved by experiment that human blood can not be infected by these species. Hence we are limited in our differential diagnosis to the tertian, quartan, and tropical parasites. Figs. 1 and 2 present no point of similarity to the product of a quartan schizogenesis; the number of chromatic particles for the merozoites is much too great, the pigment is yellow-brown and coarse, the protoplasm light violet-red, instead of light azure-blue as it should be in the quartan parasite with Giemsa's stain. Moreover, after an exhaustive examination of the blood preparation, no sign of quartan infection in the form of rings, band-like parasites, or characteristic gametes can be found; finally, fig. 2 exhibits many and fig. 1 two small Maurer's spots.

When the red blood cells are infected by ring-formed parasites, they always exhibit Maurer's spots. Since I did not find a quartan infection during the examination of the blood, we may also exclude from our discussion the parthenogenesis of the female gamete, which until now has never been observed.

A tertian schizogenesis and a parthenogenesis of the tertian macrogamete are just as readily excluded because of the morphologic aspect of the segmenting form, the staining reaction with respect to Giemsa's solution, the kind and color of the pigment, the absence of Schuffner's dots, the fact that the infected chromocytes are neither enlarged nor faded, and the lack of further tertian forms such as rings, amœbic forms, and gametes. In order to confirm the preceding view, namely, the inadmissibility of tertian parthenogenesis by comparison, I have added figs. 4 and 5, drawn with a magnification of 950 diameters. These specimens were prepared in an analogous manner and were stained with Giemsa's solution like the preparation represented by figs. 1, 2, and 3, with the difference that they were stained for a shorter time.

Fig. 4 demonstrates the first stage, where the light-blue protoplasm is separated very distinctly to the right and left. The former is the *Restkörper,* containing the expelled protoplasm destined to degenerate, a small chromatic mass, and a small quantity of pigment. The right side includes a spindle-shaped chromatic band, in which there may already distinctly be observed a differentiation in the form of the darker granules, for the subsequent segmentation of the chromosomes.

Fig. 5 represents the final stage of the parthenogenesis. The *Restkörper* is to be found situated in the upper left-hand corner with a certain amount of marginal, violet-red, chromatic substance. In the lower right-hand quadrant may be seen a light-blue sporular form, with eight chromatic particles destined for the young parasites. The *Restkörper* and segmenting form are very clearly discerned in both illustrations. Furthermore, a very marked enlargement and irregular, angular metamorphosis of the red blood cells may be distinguished in both of the figures. The cells exhibit beautiful examples of Schuffner's dots. Both forms of parthenogenesis were obtained from two of my blood slides made at Koeta-Radja two and a half years ago. These I submitted for verification to Von Prowazek, Mayer, Rodenwaldt, and Gonder, of the Institut für Schiffs und Tropen-Krankheiten at Hamburg. These observers confirmed my own conclusions.

It only remains to decide whether the forms illustrated in figs. 1 and 2 result from schizogenesis or parthenogenesis of the tropical parasite. I had an opportunity of comparing my blood slides with a long series of very characteristic schizogenesis of the tropical parasite at the Institut für Schiffs und Tropen-Krankheiten at Hamburg. The differences are very important and are as follows:

Figs. 1 and 2.	*Schizogenesis of the tropical parasite.*
(*a*) *Size.* The segmenting form fills almost the whole normal-sized red blood cell.	Segmenting forms reach a maximum of two-thirds of the size of the cell.
(*b*) *Shape.* Fig. 1: Elongated oval-shaped, with a slightly indented margin on the right and terminating in an obtuse and slightly bent point. Fig. 2: Oval with its center lying slightly outside the center of the blood cell.	Mostly circular and generally situated in or near the center of the red blood cell.
(*c*) *Chromosomes.* Large, coarse, purple-brown, peculiarly imbedded and arranged in a red-violet basic substance which is band-like in form and which extends in a curve parallel to the margin of the parasite.	Small, fine, purple, separated from one another, and distributed in a circular manner around the pigment which lies in the center.
(*d*) *Protoplasm.* Stained light blue-violet and identical with that of the crescent bodies.	Light azure-blue, including the small chromosomes more or less.
(*e*) *Pigment.* Coarse, yellow-brown, scattered, excentrically situated, quite similar to the pigment of the crescent bodies.	Fine, dark-brown or black, mostly concentrated in one clump, generally situated in the center and surrounded by the merozoites.

GENERAL CONCLUSIONS.

In view of the differences noted above, which have been investigated also by Nocht, Von Prowazek, Mayer, Rodenwaldt, and Gonder, I believe I can exclude the schizogenesis of the tropical parasite in the case in question, so that nothing remains but to admit that here we are dealing with parthenogenetic forms of the tropical macrogamete. As confirmatory evidence, I desire to emphasize the following facts:

1. The size and shape of the segmenting parasites, in which may be observed very distinctly in the upper right-hand corner of fig. 1, the obtuse, slightly bent point, the crescent body, which point may be seen much better in fig. 3, where the two poles can not be mistaken.

2. The light, blue-violet staining reaction of the protoplasm of the parasite, identical with that of the crescent bodies in the same blood preparation and entirely different from the light azure-blue coloring of the quartan and tertian parasites, which have been treated in the same way.

3. The coarse structure, size, and peculiar arrangement of the chromosomes, which for the greater part lie at right angles to the red-violet band-like basic substance.

4. The coarse, yellow-brown pigment distributed in a small group, for the most part excentrically situated and quite similar to that of the crescent bodies.

5. The absence of a mixed infection, so that only a simple tropical infection can be present.

Whereas fig. 4, with its spindle-shaped chromatic band, presents the initial stage of the parthenogenesis of the tertian macrogamete, and fig. 5, the completed segmentation, I wish to call attention to fig. 3, which shows the band-like chromatic mass in which an early division is already to be observed, analogous to the process illustrated in fig. 4. This form I consider as the earlier stage of the parthenogenesis of the tropical macrogamete, whereas figs. 1 and 2 represent the almost finished sporulating stages of the same metamorphosis. Moreover, fig. 1 in the lower left-hand quarter probably shows the *Restkörper*.

I do not conceal the fact that the form illustrated in fig. 3 was considered at Hamburg to resemble a young crescent body; nevertheless, I consider myself bound to adhere to the opinion which I have set forth in this paper, an opinion which has been arrived at only after a careful and exact comparison of this form with the young crescent bodies in the same blood slide, which latter have a totally different appearance.

ILLUSTRATIONS.

PLATE I.

FIGS. 1 to 3. Parthenogenesis of the tropical macrogamete ± 1,500 x.
FIGS. 4 and 5. Parthenogenesis of the tertian macrogamete ± 950 x.

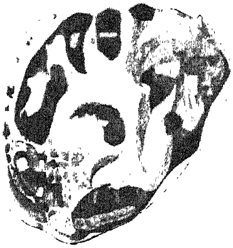

FIG. 1.

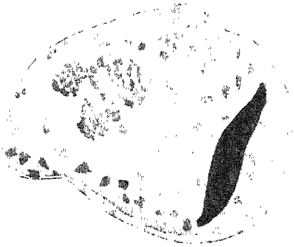

FIG. 4.

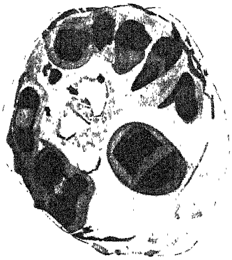

FIG. 2.

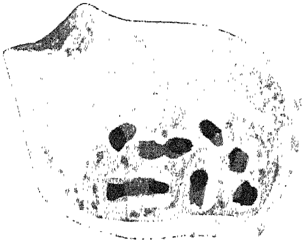

FIG. 5.

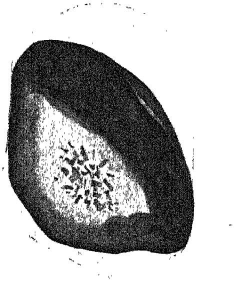

FIG. 3.

PLATE I.

ON MALARIA PARASITES OF THE ORANG-OUTAN.

By G. SHIBAYAMA.[2]

(From the Institute for Infectious Diseases, Tokio.)

The first and only investigation of the malarial parasite in the orang-outan was made by Halberstaedter and Prowazek in Java in the year 1907, while reports on the malarial plasmodium of *Maccacus* are not lacking in the literature. By a comparative study, the authors established the species diagnosis between the parasite of *Maccacus* and that of the orang-outan.

The plasmodium of the orang-outan which I have studied and which is illustrated in the accompanying plates does not differ from the *Plasmodium petheci* spec. nov. Halb. u. Prow., except in the absence of stippling (*"Zipfelung"*) of the red blood corpuscles. The young forms appear as small rings which, as in the case of the tropical parasite of man, are composed of a nucleus staining red and of a crescent-like mass of protoplasm staining blue. Ribbon-like forms resembling those of the quartan parasite of man are also observed. In the adult parasite a vacuole appears between the nucleus and the protoplasm, and rod-like pigment granules are also present. The chromatin of the nucleus enlarges and becomes differentiated as the parasite increases in size.

The sexual forms resemble the quartan parasite in respect to pigmentation and staining reactions. The male sexual forms are rich in chromatin. The protoplasm takes a paler stain and is but slightly pigmented. The female gametocytes on the contrary contain dark protoplasm and are rich in pigment. The schizogony of the parasite of the orang-outan takes place after the manner of the human tertian parasite. The nucleus of the schizonts divides into 12 to 16 parts, most of the pigment being situated in the center of the cell.

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 12, 1910. Translated from the German.

[2] Delegate from His Imperial Japanese Majesty's Government.

ILLUSTRATIONS.

PLATE I.

FIG. 1. *Plasmodium petheci sp. nov.* Ringform like the tropical plasmodium.
2. Amœboid form with vacuole.
3. Double infection.
4. Adult form with pigment granules and differentiated chromatin.
5. Microgametes like quartan parasites.
6. Macrogametes like quartan parasites.
7. Schizogony according to the type of the human tertian parasite.

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

FIG. 5.

FIG. 6.

FIG. 7.

PLATE I.

MALARIAL FEVER DURING THE PUERPERIUM.[1]

By J. M. Atkinson.[2]

When considering the subject-matter for a paper to be read before this most important gathering, containing, as it does, members from practically all the countries east of Suez, it occurred to me that some useful practical deductions might be arrived at by the discussion of the puerperium complicated by malaria. As a text for these remarks I shall give you the notes of two of the cases which have occurred in my twenty-two years of clinical experience in Hongkong.

The first was that of an English lady, who was admitted to the Maternity Hospital of the Government Civil Hospital on December 21, 1902. The patient was a primipara at full term, who stated that she had been suffering from fever for some days before admission, and that her temperature had been as high as 40.5°C. (105°F.). Though not in labor, the patient was recommended to enter the hospital at once, both on account of the fever and especially because both she and her relatives were very anxious in regard to her condition. She was admitted the same evening, and her temperature at 9 p. m. was 38.9°C. (101.6°F.). She was placed on low diet, and a diaphoretic mixture to be taken every four hours was prescribed. On the following morning her temperature was normal.

A blood film was examined at this time and simple *tertian* parasites and *ring-forms* were found. Three-tenths of a gram (5 grains) of quinine was ordered every four hours. At 6 p. m. on the evening of the 22d labor pains commenced. At 6 a. m. on the 23d her temperature was 37.8°C. (100°F.), and at 12.15 p. m. the child was born.

Beyond slight post-partum hæmorrhage, which was checked with a hot lysol douche, the labor was normal.

Quinine was continued as before. At 8 p. m. her temperature was 40°C. (104°F.). The fever was evidently due to a tertian attack, as next morning the temperature was normal. From this date there was no more fever; the quinine was continued, and on the 27th the note was made that a blood film showed some *ring-forms* but no *simple tertian* parasites.

The patient was discharged eighteen days afterwards, free from malaria, repeated blood examinations having shown no parasites.

This case is one of interest from the fact that the patient had only arrived in the colony a few months previously. She had never to her knowledge had malaria before and did not come from a malarial country.

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[1] Read at the first meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 10, 1910.

[2] Principal medical officer, Hongkong; delegate from the government of Hongkong.

During her stay in Hongkong, however, she had resided in a locality (MacDonald Road) known to be infested with *Anopheles* and where malarial fever was rife. In the previous summer extensive building operations had been carried on in this district of the town, many European houses having been built there, and malarial fever was very prevalent. In the Annual Report of the Medical Department for the year 1902[3] I find, under the heading "Antimalarial measures," the following:

> This locality had been especially dealt with, much undergrowth had been removed, pools of stagnant waters had been drained, and the *nullahs* partially trained. In the winter months a general fumigation of the servants' quarters in the houses of this district was carried out by the sanitary board staff with the object of killing off the *Anopheles* and their ova.

In this case immediate blood examination revealed the cause of the fever, and the subsequent rise of temperature after labor caused no anxiety as to sepsis. The blood examination also enabled the attending physician to ease the mind of the patient and assure her relatives as to the favorable prognosis of the case.

The history of the next case is one in which an attack of malarial fever induced premature labor. It occurred as recently as November last and the history is briefly as follows:

> On November 27 last I received a telephone message that a case of premature labor was being sent to the Victoria Hospital for Women and Children from Stonecutters' Island.
>
> I must mention that arrangements have been made whereby the women and children from the military, when sick, are sent to this hospital.
>
> At 3.45 p. m. that day I received a note from the sister on duty stating that "the patient had just arrived, looking very ill, her temperature being 40°C. (104°F.) and pulse 128. She complained of severe headache, great thirst, and had severe pain in the right side. The perineum was ruptured, very much swollen, and tender to the touch."
>
> I sent word that the patient should be admitted to the isolation ward, as the hospital was rather full, there being several recent confinement cases under treatment. It appeared to me that the case might be one of acute puerperal sepsis.
>
> On examination I found the patient to be an English woman with a small, eight-months' baby, weighing but 2 kilos (4½ pounds). Her condition was as described by the sister; in addition, she had a brown, dry tongue and was complaining of severe headache.
>
> She was the wife of a sergeant in the Royal Garrison Artillery and had been in Hongkong for two years, during the whole of which time she had been living in the married quarters at Stonecutters' Island, situated in the harbor some 3 miles from Victoria.
>
> Eighteen months before she had suffered from an eight weeks' abortion, otherwise her medical history was good and she had not previously had malarial fever.
>
> As she was so ill I did not disturb her further that night, but gave her 1 gram (15 grains) of trional and ordered fomentations of corrosive sublimate to be applied to the swollen, torn perineum. The following morning the patient had

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[3] Report of the Principal Civil Medical Officer for the year 1902, p. 264.

improved; she had slept well, the headache was gone, and her temperature and pulse were normal. The swelling of the perineum was much less marked and the lochia were not offensive.

I then questioned her as to her illness and she informed me that the fever had commenced suddenly with an attack of shivering on the 25th of the month. On the 26th labor pains set in, and the child was born at 3 a. m. on the 27th. A military doctor had seen her and immediately ordered her removal to Hongkong. This necessitated her traveling by a launch for over an hour, and then being transferred on a stretcher to the Victoria Hospital, some 1.000 feet above the sea level. Naturally, she arrived in a somewhat collapsed condition, but soon rallied on being placed in a warm bed and after being given some stimulant. The pain she described in her right side was evidently muscular.

On examining her blood on the morning of the 28th, I found it to be swarming with benign tertian parasites. She was given 0.3 gram (5 grains) of quinine every four hours, together with an effervescing mixture containing 4 minims of dilute hydrocyanic acid to help her to retain the drug. As the swelling of the perineum had subsided, I removed several small sloughs and inserted a deep silkworm suture under cocaine anæsthesia. Her temperature did not rise again to 37.8°C. (100°F.), and she made an uninterrupted recovery. On January 3 she was discharged from the hospital quite well, accompanied by her baby, who then weighed 3 kilos (6⅗ pounds).

Both these cases might have caused considerable anxiety to the medical attendant had they not occured in a malarial country where the physician was alert for this complication. So much does malaria complicate practically all illnesses in Hongkong, especially in the hot summer months, that it is a rule with us to give parturient cases quinine whenever there is the smallest rise of temperature after labor. The practical question must also be considered of how far one is justified in giving quinine daily as a prophylactic to women during the period of pregnancy. Many physicians are chary of doing so, as they think it may from its ecbolic action on the uterus induce abortion or premature labor. In my opinion, it is malarial fever that is more likely to produce that effect, and I am in the habit of always advising the daily dose of 0.130 gram (2 grains) during the summer months, especially to pregnant women whom I have known to have been subject to attacks of malarial fever.

The following is quoted from Dr. Albert H. Smith:[4]

> Quinine has no power in itself to excite uterine contractions, but simply acts as a general stimulant and promoter of vital energy and functional activity. In normal labors at full term, its administration in a dose of 15 grains is usually followed in as many minutes by a decided increase in the force and frequency of the uterine contractions, changing in some instances a tedious exhausting labor into one of rapid energy, advancing to an early completion.

Quinine promotes the permanent tonic contraction of the uterus, after the expulsion of the placenta. Women that had flooded in former labors escaped entirely, there not having been one instance of post-partum hæmorrhage in 42 cases so treated. It also diminished the lochial flow where it had been excessive in former labors, the change being remarked upon by the patients; it consequently lessens the severity of the after pains. Cinchonism is very rarely observed as an effect of large doses in parturient women.

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[4] *Trans. Coll. Phys. Philadelphia* (1875), 183.

I have discussed this question of the supposed echolic physiological action of quinine with several of the medical practitioners in Hongkong and they agree with me that this action is very slight; some, in concurrence with myself, doubt that it has any effect in this way, and I am inclined to believe with Dr. Albert Smith that it acts more as a general stimulant and promoter of vital energy and functional activity. Of one thing I am convinced, and that is that when quinine is administered in malarial fever it expends its energy in killing the plasmodium and does not produce any deleterious effects on the system.

The large doses of quinine which are sometimes required seem extraordinary, but these doses can be given with impunity in some of those malignant cases of malarial fever which every physician who practices in malarial countries has occasionally to deal with.

Similarly, large doses of other drugs are sometimes necessary in certain other diseases and are tolerated by the economy. I need only instance mercury in the treatment of syphilis and arsenic in the treatment of certain forms of anæmia.

TROPICAL BRONCHOMYCOSIS. OBSERVATIONS ON A NEW SPECIES OF EPIDERMOPHYTON FOUND IN TINEA CRURIS. A NEW INTESTINAL SPIRILLUM.[1]

By Aldo Castellani.[2]

TROPICAL BRONCHOMYCOSIS.

During the six years of my residence in Ceylon I have often been struck by the comparatively large number of cases of subchronic and chronic bronchitis which the physician on superficial clinical examination would suspect to be of a tubercular nature, while complete investigation shows constant absence of tubercle bacilli in the sputum. The ophthalmic and cutaneous reactions are negative, and inoculations of the sputum into susceptible animals are also negative. Some of these proved to be cases of bronchospirochætosis, the condition described by me in 1905. In other instances, however, neither spirochætæ nor tubercle bacilli are found, and in a certain number fungi more highly organized than bacteria are present. These are cases of bronchomycosis. I have encountered at least 20 cases of this affection in Ceylon, basing the diagnosis on the result of the microscopic examination, and have culturally studied the fungi isolated from 4 cases. In Ceylon a mild and a graver type of this disease may be distiguished. In the mild type the patient complains of cough with mucopurulent expectoration. There is no fever, the general condition is fairly good; the physical examination of the chest will show nothing at all, or a few moist and dry râles. In the severe type, the disease closely resembles phthisis, the patient becomes emaciated, there is hectic fever, mucopurulent and bloody expectoration; the physical examination of the chest reveals patches of dullness, fine crepitations and pleural rubbing. I may cite a few instances of each type.

Case 1 (*mild type*).—Mr. B. A., young European, occupation tea-taster, has been in Ceylon eight years, has had no disease of importance. He remains several hours daily in rooms full of tea dust and fluff and says that he often snuffs various teas, putting a pinch of the tea in his nostrils. For six months he has complained of a cough with a certain amount of mucopurulent expectoration. No fever. The examination of the chest reveals nothing. Microscopic examination of the sputum for tubercle bacilli is negative. In fresh preparations a few branching mycelial tubes are visible; very few free spores.

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 12, 1910.

[2] Professor of tropical medicine and lecturer on dermatology, Ceylon Medical College; delegate from the government of Ceylon.

Treatment: Ordinary cough mixtures were useless; potassium iodide in large doses cured the condition in four weeks.

Case 2 (mild type).—Mr. S. A., European planter; is compelled to remain for a couple of hours daily in the tea factory. He consulted me in September, 1909, and informed me that he was suffering from what the planters call "tea-factory cough." He had mucopurulent expectoration; no fever; his general condition was fairly good. The microscopic examination of the sputum for tubercle bacilli was negative. Numerous spores and mycelial tubes of an oïdium-like fungus were present.

Treatment: Potassium iodide in 1.0 gram (15 grains) doses four times daily cured him in three weeks.

Case 3 (severe type).—Mr. M., a planter. The sputum had been examined many times for tubercle bacilli by his medical attendants with negative results. When the patient arrived in Colombo he was extremely weak. He had serotine fever, bloody expectoration, fine crepitations and pleural rubbing on both sides. I examined the sputum many times for tubercle bacilli with negative results. Inoculation into guinea pigs was negative. Fresh preparations always showed numerous spores and some mycelial threads. Cultures were made from the sputum on agar and on various sugar media. The only germ grown was a hyphomycete which showed the same morphological characters as that present in the fresh preparation, and a streptococus. The patient became gradually worse. The cough was not relieved by guaiacol, duotol, nor by potassium iodide. He died three weeks after arrival.

Case 4.—Singhalese convict in Mahara jail, near Colombo. The symptoms of his disease were at first obscure, and various diagnoses, including typhoid, malaria, and phthisis, were suggested. The sputum was sent to me several times, but tubercle bacilli were always absent. Instead, a saccharomyces and oïdium-like fungus were found. The patient was later transferred to the clinic for tropical medicine where I kept him under observation for two months. The cough slowly decreased and finally stopped, the fever completely disappeared. His blood by means of Widal's reaction was shown to contain agglutinins for the cultures of the oïdium-like fungus, and the saccharomyces.

BACTERIOLOGICAL INVESTIGATION OF THE FUNGI FOUND IN THE FOUR CASES.

In four cases I plated from the expectorations and grew the hyphomycetes. In the case from the Mahara jail, as I briefly stated, two fungi were present—a saccharomyces and an oïdium—in the other three cases only oïdium-like fungi were observed.

Description of the saccharomyces.—In fresh preparations of the sputum the organism appeared as oval, rounded budding cells. It was Gram positive. The cultural characteristics are summarized in the following table.

The cultural characters of the saccharomyces at 37°C.

Medium.	Per cent.	Characters.
Glucose-litmus broth	2	Acid and gas. Thick pellicle.
Lævulose-litmus broth	1	Do.
Maltose-litmus broth	2	Practically no change. Thick white pellicle.
Galactose-litmus broth	1	Do.
Saccharose-litmus broth	2	Do.
Lactose-litmus broth	2	Do.
Mannite-litmus broth	2	Do.
Dulcite-litmus broth	2	Do.
Dextrin-litmus broth	1	Do.
Raffinose-litmus broth	1	Do.
Arabinose-litmus broth	1	No change. Delicate pellicle.
Nutrose-litmus broth	1	No change. Very delicate pellicle.
Inulin-litmus broth	1	Practically no change. Thick white pellicle.
Adonite-litmus broth	1	No change. Delicate pellicle.
Litmus milk		No change.
Broth		Clear, thin pellicle. Slight sediment at bottom of tube.
Peptone-water		Clear, slight sediment at bottom of tube. Practically no growth.
Serum		White growth. Not liquefied.
Agar		Delicate whitish growth. (Delicate on saccharose and acid maltose-agar.)
Glucose-agar		Very thick growth.

Description of the oïdium-like fungi.—In fresh preparations of sputum, septate mycelial tubes 3 to 4 μ in breadth were seen at the terminal end of each, of which two to four shorter ovoid elements could often be observed; numerous free, oval, roundish spores 4 to 8 μ were also seen. The organism was positive for Gram's stain. On ordinary agar and various sugar agars the fungi grew abundantly, producing roundish, thick, white, creamy colonies which later coalesce. The cultural characteristics in various sugar media are collected in the following table, in which for comparative purposes those of the saccharomyces are repeated.

The cultural characters of oïdium (strain 1) at 37° C.

Medium.	Per cent.	Characters.
Glucose-litmus broth	2	Acid and gas. No pellicle. Abundant growth at bottom of tube.
Lævulose-litmus broth	1	Do.
Maltose-litmus broth		Acid. Gas in 2 days. No pellicle. Abundant growth at bottom of tube.
Galactose-litmus broth	1	Acid and very slight gas. No pellicle. Fairly abundant growth at bottom of tube.
Saccharose-litmus broth	2	Acid and gas. No pellicle. Abundant growth at bottom of tube.
Lactose-litmus broth	2	No change. Very slight growth at bottom of tube.
Mannite-litmus broth	2	Do.
Dulcite-litmus broth	2	Do.
Dextrin-litmus broth	1	No change. Fairly abundant growth at bottom of tube.
Raffinose-litmus broth	1	No change. Very slight growth at bottom of tube.
Arabinose-litmus broth	1	No change. Fairly abundant growth at bottom of tube.
Nutrose-litmus broth	1	No change. Slight growth at bottom of tube.
Inulin-litmus broth	1	No change. Very slight growth at bottom of tube.
Adonite-litmus broth	1	No change. Fair growth at bottom of tube.
Litmus milk		No change.
Broth		Clear. Fine (thin) pellicle. Slight sediment.
Peptone water		Clear. Thin pellicle. Slight sediment.
Serum		Creamy growth, surrounded by a zone of yellowish-pink color. Not liquefied.
Agar		Thin white moist growth.
Glucose-agar		Very thick wax-like growth. (Also very thick on saccharose and acid maltose-agar.)

The cultural characters of oïdium (strain 2) at 37° C.

Medium.	Per cent.	Characters.
Glucose-litmus broth	2	Acid and gas. No pellicle. Good growth.
Lævulose-litmus broth	1	Do.
Maltose-litmus broth	2	Do.
Galactose-litmus broth	1	Acid and gas. No pellicle. Fair growth.
Saccharose-litmus broth	2	Acid and gas. No pellicle. Good growth.
Lactose-litmus broth	2	No change. Slight growth at bottom of tube.
Mannite-litmus broth	2	Do.
Dulcite-litmus broth	2	Do.
Dextrin-litmus broth	1	No change. Fair growth at bottom of tube.
Raffinose-litmus broth	1	Do.
Arabinose-litmus broth	1	Do.
Nutrose-litmus broth	1	Do.
Inulin-litmus broth	1	Do.
Adonite-litmus broth	1	Do.
Litmus milk		No change.
Broth		Clear. Very slight pellicle. Practically no growth.
Peptone water		Clear. Practically no growth.
Serum		Growth white and shining with the serum under the growth and immediately surrounding it of a distinct reddish color. Not liquefied.
Agar		Very thin white growth.
Glucose-agar		Thick growth. White waxy surface. (Also very thick on saccharose and acid maltose-agar.)

The cultural characters of oïdium (strain 3) at 37° C.

Medium.	Per cent.	Characters.
Glucose-litmus broth	2	Acid and gas. No pellicle. Good growth at bottom of tube.
Lævulose-litmus broth	1	Do.
Maltose-litmus broth	2	Do.
Galactose-litmus broth	1	Acid in 5 days. No gas.
Saccharose-litmus broth	2	Acid and gas in 5 days.
Lactose-litmus broth	2	No change. Very slight growth at bottom of tube.
Mannite-litmus broth	2	Do.
Dulcite-litmus broth	2	Do.
Dextrin-litmus broth	1	Do.
Raffinose-litmus broth	1	Do.
Arabinose-litmus broth	1	Do.
Nutrose-litmus broth	1	Do.
Inulin-litmus broth	1	Do.
Adonite-litmus broth	1	Do.
Litmus milk		No change.
Broth		Clear. Slight sediment. Practically no growth.
Peptone water		Do.
Serum		White growth. Slight pigmentation surrounding bottom of growth after 10 days. Not liquefied.
Agar		Very thin white growth.
Glucose-agar		Thick white wax-like growth. (Also very thick on saccharose and acid maltose-agar.)

The cultural characters of oïdium (strain 4) at 37° C.

Medium.	Per cent.	Characters.
Glucose-litmus broth	2	Acid and gas. No pellicle. Good growth at bottom of tube.
Lævulose-litmus broth	1	Do.
Maltose-litmus broth	2	Do.
Galactose-litmus broth	1	Acid. No gas. No pellicle. Good growth at bottom of tube.
Saccharose-litmus broth	2	Acid. No pellicle. Good growth at bottom of tube. Slight gas at eleventh day.
Lactose-litmus broth	2	No change. Good growth at bottom of tube.
Mannite-litmus broth	2	Do.
Dulcite-litmus broth	2	Do.
Dextrin-litmus broth	1	Do.
Raffinose-litmus broth	1	Do.
Arabinose-litmus broth	1	Do.
Nutrose-litmus broth	1	Do.
Inulin-litmus broth	1	Do.
Adonite-litmus broth	1	Do.
Litmus milk		No change.
Broth		Clear. Slight sediment. Practically no growth.
Peptone water		Do.
Serum		Whitish growth. Not liquefied.
Agar		Thin white moist growth.
Glucose-agar		Very thick wax-like growth. White. (Also very thick on saccharose and acid maltose-agar.)

Cultural reactions at 37° C. after fourteen days.

[A.=production of acid; G.=production of gas; O=no change.]

	Glucose.	Laevulose.	Maltose.	Galactose.	Saccharose.	Lactose.	Mannite.	Dulcite.	Dextrine.	Raffinose.	Arabinose.	Nutrose.	Inulin.	Adonite.	Litmus milk.	Broth.	Peptone water.	Liquefaction of serum.	Liquefaction of gelatine.	Indole.
Oïdium strain I	A. G.	A. G.	A. G.	A. G.[a]	A. G.	0	0	0	0	0	0	0	0	0	0	[b]0	[b]0	0	0	0
Oïdium strain II	A. G.	A. G.	A. G.	A. G.	A. G.	0	0	0	0	0	0	0	0	0	0	[b]0	[c]0	0	0	0
Oïdium strain III	A. G.	A. G.	A. G.	A.	A. G.	0	0	0	0	0	0	0	0	0	0	[c]0	[c]0	0	0	0
Oïdium strain IV	A. G.	A. G.	A. G.	A.	A.	0	0	0	0	0	0	0	0	0	0	[c]0	[c]0	0	0	0
Saccharomyces	A. G.	A. G.	0	0	0	0	0	0	0	0	0	0	0	0	0	[b]0	[c]0	0	0	0

[a] Very slight gas. [b] Thin pellicle. [c] Practically no growth.

It will be seen from the table that the four strains of oïdium isolated are identical in all their cultural characteristics except that numbers 1 and 2 produce acid and gas in galactose, while strains 3 and 4 produce only acid. This has always remained constant, although I have repeated the reactions several times. All the four strains are different from the ordinary *Oïdium albicans* and *Oïdium lactis,* as they have no action on milk, at least within three weeks. As regards the saccharomyces, its cultural characteristics are different, as far as I know, from any other saccharomyces as yet described.

CONCLUSIONS.

1. A type of bronchomycosis in which oïdium-like and saccharomyces-like fungi are found is not rare in Ceylon. The condition might be called bronchooïdiomycosis, or more briefly bronchooïdiosis.

2. Two types of the condition may be clinically distinguished, a mild and a severe one; the latter closely resemblies phthisis. The mild type is apparently amenable to treatment with potassium iodide.

3. The strains of oïdia found in my cases are different from the ordinary *Oïdium albicans* and *Oïdium lactis,* as they do not affect milk.

4. All the strains found by me are identical in all respects, except that some produce gas in galactose and others do not. For the oïdium which produce gas in galactose I propose the name *Oïdium tropicale;* for the saccharomyces I suggest the name *Saccharomyces krusei.*

5. The diagnosis of bronchooïdiosis can be made only by bacteriologic methods. It is differentiated from phthisis by the absence of tubercle bacilli and the negative animal inoculations; from bronchial spirochætosis by the absence of spirochætæ; and from endemic hæmoptysis by the absence of the ova of the trematode.

6. Care should be taken before making the diagnosis of bronchomycosis that the sputum is collected in sterile vessels and examined as soon as possible, because sputa left exposed to the air frequently become contaminated in the Tropics with various species of nonpathogenic saccharomyces and oïdia. Primary bronchomycosis should be also differentiated from those cases of chronic debilitating disease in which *Oïdium albicans* spreads from the mouth to the bronchi.

OBSERVATIONS ON A NEW SPECIES OF EPIDERMOPHYTON FOUND IN TINEA CRURIS.

In 1905 I separated dhobie itch from the ordinary forms of tinea corporis and Macleod suggested for the affection the term tinea cruris. I stated at the time that the eruption was caused by different species of fungi, the commonest of which a few months later I termed *Trichophyton cruris.* Pernet found and described a fungus from a case of tinea cruris, and later I gave the name of *Tr. perneti* to this species. In 1907 Sabouraud made an investigation into an epidemic of tinea cruris occurring in France and he also came to the conclusion that tinea cruris, or, as he prefers to call it, tinea inguinalis, should be separated from tinea corporis. He created a new genus for the trychophyton-like organism observed in the disease—*Epidermophyton.* The principal characteristics of this genus are that the fungi do not attack the hair follicles, do not produce suppuration, and that cultures show forms of degeneration in a very short time. Sabouraud isolated only one species in all of his cases; but in the Tropics, in my experience, there can not be any doubt of the plurality of species of the fungi producing tinea cruris or dhobie itch. The fungi described so far are:

1. *Epidermophyton cruris* Castellani, 1905. *E. inguinale* (Sabouraud), 1907. Colonies in maltose agar whitish, occasionally orbicular; later showing a greenish color.

2. *Epidermophyton perneti* Castellani, 1907. *Trychophyton perneti.* Colonies in maltose agar of a delicate pinkish color. The pinkish color is lost in subcultures.

To these two species I am now in position to add a third, which I will designate as *E. rubrum* and which I have isolated from two cases of the so-called eczematoid type of tinea cruris. In one patient the eruption was localized to the groins, scrotum and thighs; in the other, besides the scrotum and thighs the armpits and portions of the chest and abdomen were affected. I may here remark that tinea cruris is not always localized in the groins or the armpits. The affection generally begins in these regions, but in many cases it may spread to any other part of the body except the scalp; indeed I have seen a few cases in which the disease started on the chest, arms, or face, and then spread to the groin and armpits.

DESCRIPTION OF THE FUNGUS.

In preparations from the affected parts in potassium hydroxide mycelial tubes and free spores are observed, identical to those seen in *E. cruris* and *E. perneti*, and similar to those of any *Trychophyton* of the megalosporon type. The spores are large, globular, 4 to 6 μ in diameter, with a double contour. The mycelial tubes, 2 to 3.5 μ, are straight, bent, or variously shaped.

CULTURES.

Sabouraud agar.—The growth begins to appear four to six days after inoculation as a raised, red spot which gradually enlarges. The full-grown colonies are of a deep red color, either with a central knob or crater form, and are partly covered, especially the central knob, by a white down. In old cultures this may cover the entire growth and may hide the red pigmentation almost completely. The pigmentation even as far as the nineteenth subculture has not been lost.

Glucose agar.—The cultures are of a very deep blood-red color, and portions of the medium take the same tint. In old cultures a large amount of white down is present over the entire surface of the growth, but scraping this out, the red pigmentation is then extremely well marked. The red pigmentation at the time of writing is still characteristic in the nineteenth transplanted subculture.

Mannite.—Colonies deep red, covered with white down and with central knob. After a time the whole surface of the growth shows abundant, whitish fluff.

Maltose.—In 2 per cent maltose agar, alkaline or acid, the colonies are whitish; in 4 per cent maltose agar they may occasionally be red.

Ordinary agar.—The fungus grows well, white colonies with a central knob being formed; later on these show a peripheral greenish ring, encircled by a thin whitish or whitish-green zone.

Saccharose agar.—A central white knob and later a yellowish ring are green, finally a whitish zone forms at the periphery.

Glycerine agar.—White growth with central white knob and white powdery surface.

The principal cultural characteristics already described and those presented in other media are collected in the following table.

The principal cultural characters of epidermophyton rubrum.

Medium.	Per cent.	Characters.
Sabouraud agar		Red growth.
Glucose agar	2	Deep red growth with later white fluffy surface.
Mannite agar	2	Do.
Saccharose agar	2	Cream growth with white, powder-like surface.
Maltose acid agar	2	Do.
Maltose alkali agar	2	Do.
Lactose agar	2	Do.
Glycerine agar	2	Do.
Saccharine agar	2	White growth with white, powder like surface. (After 1 month the growth on saccharose presented a white central knob surrounded by a grayish-white zone. This grayish-white zone was surrounded by a distinct yellow ring and outside this was another zone of gray white color.)
Agar (plain)		As saccharine.
Gelatine		White growth. Nonliquefied after 21 days.
Serum		Nonliquefied after 21 days.
Litmus milk		Alkaline. Complete separation in 7 days.
Broth		Growth on surface and at bottom of tube of pale yellow color.
Peptone water		Growth at bottom of tube. White.
Lactose-litmus broth	2	No acidity. Good surface growth of greenish-white color.
Mannite-litmus broth	2	No acidity. Good surface growth. White.
Dulcite-litmus broth	2	No acidity. Good growth at bottom of tube.
Glucose-litmus broth	2	No acidity. Good surface growth. Red with whitish down.
Maltose-litmus broth	2	No acidity. Superficial whitish growth.
Saccharose-litmus broth	2	No acidity. Superficial greenish-white growth.
Lævulose-litmus broth	2	No acidity. Abundant greenish-white surface growth.
Inulin-litmus broth	2	No acidity. Abundant greenish-yellow surface growth.
Raffinose-litmus broth	2	No acidity. Abundant greenish-white surface growth.
Galactose-litmus broth	2	No acidity. Abundant greenish-yellow surface growth.
Dextrin-litmus broth	2	No acidity. Only slight growth at bottom of tube, none on surface.
Arabinose-litmus broth	2	No acidity. Greenish-white surface growth.
Adonite-litmus broth	2	No acidity. Growth only at bottom of tube and very slight.
Nutrose-litmus broth	2	No acidity. Growth at bottom of tube and also abundant surface growth of greenish-yellow color.

Observations on subcultures.—Subcultures from a Sabouraud or glucose culture on Sabouraud or glucose media are deep red, like the original cultures, but subcultures on agar, saccharine agar, and saccharose agar are white, greenish or yellowish. Subcultures from an agar culture (white) or ordinary agar, saccharine, and saccharose are white, but if Sabouraud agar tubes or glucose or mannite tubes be inoculated from a white agar colony, the fungus will not be white, but deep red. The development of the color of the fungus is therefore dependent upon the composition of the medium on which it is inoculated. In Sabouraud and mannite, and best of all in glucose media, the fungus so far as I have observed is red. At the present time I have the tenth generation and the fungus has the same characteristics as in the first.

Hanging drop cultures.—Hanging drop cultures in Sabouraud maltose or ordinary broth present the characteristics of the other *epidermophytons.* Reproduction takes place by budding and branching of the mycelial tubes; clamydospores are present. It is interesting to note the rarity of lateral conidia.

CONCLUSIONS.

1. Tinea cruris or dhobie itch is caused by several species of *Epidermophyton.*

2. The *Epidermophyton* I have described above may be added to the two already known, *Epidermophyton cruris* Castellani and *E. perneti* Castellani. For this new species I propose the name *E. rubrum.*

3. *Epidermophyton rubrum* is characterized principally by the deep red pigmentation of its growth in glucose, Sabouraud, and mannite agars; whereas it is white in ordinary agar. The pigmentation is remarkably persistent and continues to be quite characteristic at the time of writing (February, 1910), although the fungus has already been transplanted nineteen times in subculture.

A NEW INTESTINAL SPIRILLUM.

I have recently encountered two cases of a peculiar type of acute, fatal enterocolitis showing intermediate symptoms between dysentery and cholera. Some of the stools were serous and cholera-like; others consisted practically of mucus only. There was no blood. Both cases died within forty-eight hours. In one, the disease was said to have begun after eating dried fish. The stools, collected in sterile Petri dishes, were examined for *Vibrio choleræ,* with negative results. On the other hand, 85 per cent of the colonies which developed on bile-salt agar and ordinary agar were of a peculiar spirillum; the others resembled organisms of the colon group.

DESCRIPTION OF THE SPIRILLUM.

Morphology.—The spirillum varies greatly in length and in shape; the same preparation from an agar or broth culture will show some individuals 20 to 40 μ in length with 2 to 4 coils, and also short bacillary or comma-like forms. The difference in shape is so great that at first I believed I had encountered an instance of symbiosis between a bacillus and a spirillum, but even by plating and replating I never succeeded in separating the two forms, and therefore I consider them to be of one and the same organism. The spirillum is readily stained with the usual aniline dyes. It is Gram negative.

Cultural characteristics.—The cultural characteristics are given in the following table.

Cultural characteristics of the spirillum.

Medium.	Per cent.	Characters.
Litmus milk		No acidity. (After 8 weeks the milk was distinctly alkaline and peptonized.)
Broth		General turbidity; pellicle.
Peptone water		General turbidity; slight pellicle
Gelatine		Not liquefied.
Serum		Do.
Agar		Whitish. Coli-like.
Lactose-litmus broth	2	No change. Fair growth.
Saccharose-litmus broth	2	Do.
Dulcite-litmus broth	2	Do.
Mannite-litmus broth	2	Do.
Glucose-litmus broth	2	Do.
Maltose-litmus broth	2	Do.
Dextrin-litmus broth	1	Do.
Raffinose-litmus broth	1	Do.
Arabinose-litmus broth	1	Do.
Adonite-litmus broth	1	Do.
Inulin-litmus broth	1	Do.
Nutrose-litmus broth	1	Do.
Galactose-litmus broth	1	Do.
Lævulose-litmus broth	1	Do.
Indol		Negative.
Gram		Negative. Very motile.

Pathogenicity.—The spirillum was pathogenic for guinea pigs and rabbits during the first two weeks after its isolation, the animals dying in from twenty-four to forty-eight hours after hypodermic injection of 2 cubic centimeters of a broth culture or of 1 cubic centimeter intraperitoneally. After being isolated for a longer time, the organism lost its pathogenicity.

CONCLUSION.

The cultural characteristics show the spirillum most probably to be a new species, for which I propose the name of *Spirillum zeylanicum*.

ILLUSTRATIONS.

PLATE I. Bronchooïdiosis. Preparation of sputum stained by Leishman's method.
II. Epidermophyton rubrum, sp. nov. Fig. 1. Sabouraud's agar. Fig. 2. Saccharose agar.

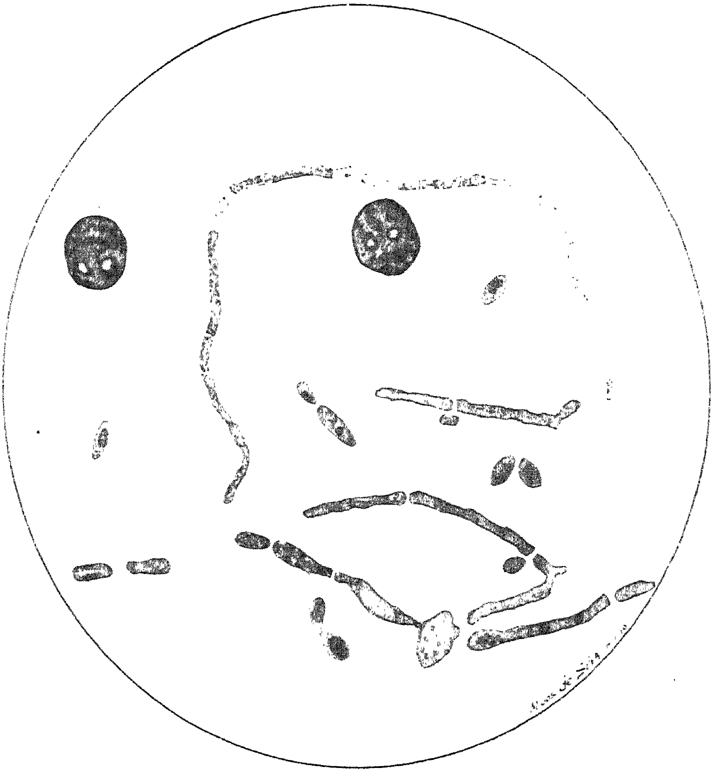
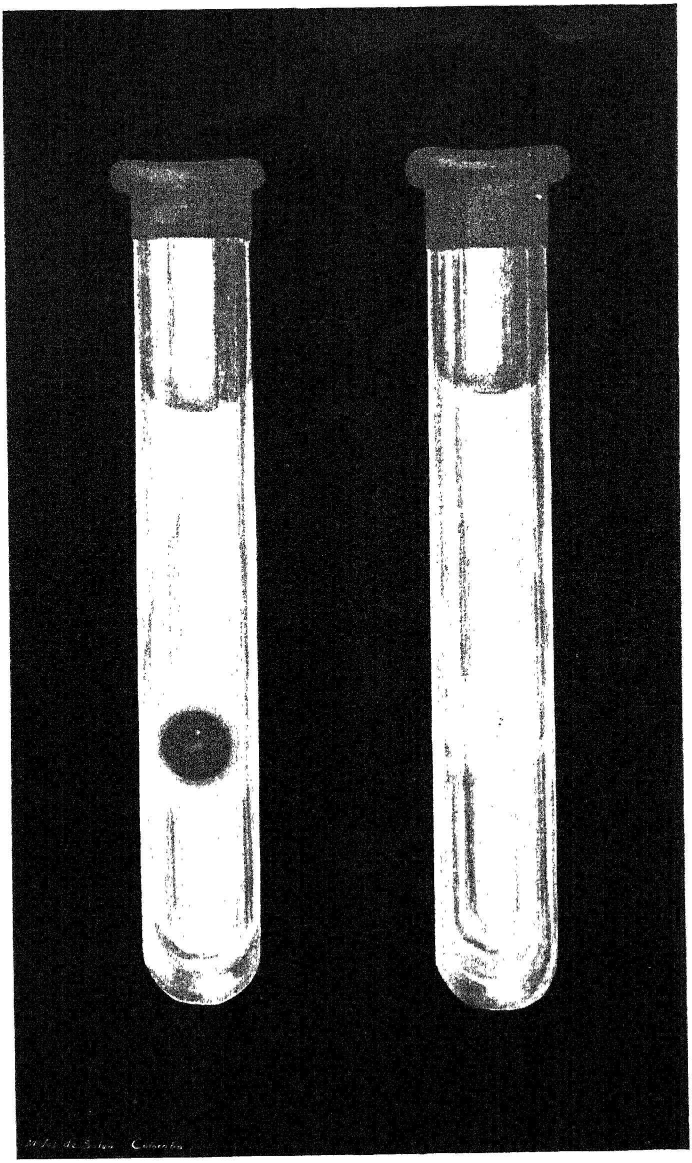


PLATE I.



M. Jos. de Silva Colombo

FIG. 1. FIG. 2.

PLATE II.

NOTE ON AN INTESTINAL FLAGELLATE IN MAN.[1]

By Aldo Castellani[2] and Albert J. Chalmers.[3]

Recently we have observed a flagellate in the stools of cases of agchylostomiasis suffering with diarrhœa. A brief description of the organism is as follows:

Fresh preparations.—The parasite is extremely motile in fresh preparations from the liquid stools. Two forms are generally present—a slender, and a larger, more rounded one. It measures about 8 to 15 μ in its greatest diameter, but the shape varies very much because the parasite is capable of amœboid movements, although no true pseudopodia are emitted. Two long flagella originate from one pole by means of which locomotion takes place. There is no evidence of any undulating membrane nor of contractile vacuoles. The protoplasm is homogeneous, but a few vacuoles may be observed in fresh preparations. The nucleus is not visible.

Stained preparations.—In preparations stained by Romanowsky's method the parasites appear globular, nearly round, or pear-shape, and the protoplasm is of a bluish color; a small, rather eccentric, approximately round nucleus is visible, which is rich in chromatin. In some individuals one or more other small chromatic granules may be observed in the protoplasm in addition to the nucleus. One of these chromatic masses often is situated close to that pole of the parasite from which the flagella originate. In successful preparations two flagella are visible which stain a pinkish or purplish color.

Cultures.—The flagellate can be grown in symbiosis with bacteria in various liquid media and in the water of condensation of several solid media.

Acid agar, maltose-agar, serum.—The organism remains alive three or four days in the water of condensation of the tubes inoculated directly from the stools, but it does not multiply and cultivation generally does not succeed in transplantation.

Saccharose agar.—The parasite remains alive for several days, but subcultures fail in the majority of cases.

Sabouraud's agar, acid maltose-agar (2 to 4 per cent), albumen-agar lactose-agar (2 to 4 per cent).—The parasite remains alive and multiplies in the water of condensation for from eight to ten or more days. Subcultures are successful. At present we have the thirty-second subculture and the parasite apparently grows as vigorously as it did four months ago. We made subcultures of the original strain every three or four days.

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[1] Read at the first meeting of the Far Eastern Association of Tropical Medicine held at Manila, March 12, 1910.

[2] Professor of Tropical Medicine and Lecturer on Dermatology Ceylon Medical College; delegate from the government of Ceylon.

[3] Registrar and Lecturer on Pathology and Animal Parasitology, Ceylon Medical College.

Nutrose-agar (2 to 4 per cent).—Probably this is the best medium. The flagellate remains alive for more than two weeks in the water of condensation, and in this medium it appears to be capable of being taken in subculture for an indefinite number of transplants. The tubes should not be capped. We generally make subcultures of the parasite twice a week.

Broth peptone water.—The flagellate dies out within two or three days in the tubes inoculated directly from the stools or from cultures.

Albumin salt solution.—The parasite may be kept alive for a long time in Grassi's albumin salt solution (albumin, 10 cubic centimeters; 5 per cent salt solution, 90 cubic centimeters).

Nutrose broth (2 to 4 per cent).—The germ multiplies and is capable of being transplanted for an indefinite number of times.

CONCLUSION.

In the stools of patients in Ceylon suffering from agchylostomiasis we have observed a flagellate which is pear-shaped or rounded, measuring from 8 to 20 μ in diameter, possessing two flagella, an undulating membrane, and capable of amœboid movements. It is easily cultivated together with bacteria on several media, the best of which is apparently nutrose-agar or nutrose broth. The developmental stages and the methods of reproduction have not as yet been studied and therefore the exact zoölogical position of the parasite can not be defined. We propose to classify it provisionally under the genus *Bodo* and to name it *Bodo asiaticus.*

In two cases in which *Bodo asiaticus* was present another flagellate was also observed. We were not able to cultivate this organism. It is rounded or fusiform, measuring 10 to 15 μ in length, with one flagellum originating at each pole. In fresh preparations it is actively motile. It may present vacuoles, but these are not contractile. In stained preparations a well-marked, though small nucleus which is rich in chromatin, can be distinguished.

ILLUSTRATION.

PLATE I. *Bodo asiaticus* sp. nov.

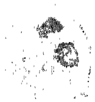

PLATE I.

SOME CLINICAL ASPECTS OF MYCETOMA, AN UNUSUAL FORM OF CALLOSITY COMPLICATING IT.[1]

By A. Hooton.[2]

The Province of Kathiawar, on the west coast of India, to which the following observations refer, is noted for the prevalence of mycetoma. During the past two years 26 cases have come under my observation. How this incidence contrasts with hospitals in other regions markedly affected by the disease I am not aware, but it is very much in excess of the prevalence in any other station of which I have personal experience. An interesting feature in this connection is the coincidence of actinomycosis in the same area. At the Medical Congress held in Bombay last year I reported two cases of that disease, which, so far as I know, has only been once previously noted in India in man, namely, by Doctor Powell, about ten years ago in Assam. There is so much in common pathologically between mycetoma and actinomycosis that it is not surprising to find them occurring in the same district. Indeed, it is somewhat remarkable that this is not more often the case.

Another unusual condition which impressed me early in my service at the Rajkot Hospital, was a type of multiple callosity which I do not remember to have seen elsewhere. Unlike the ordinary corn, these callosities occur in parts of the sole not especially subject to pressure, and they are also very much more extensive, so that in order to extirpate them it is often necessary to excavate quite a large quantity of tissue. My present observations are based partly on these callosities and their occurrence side by side with mycetoma, and I think that the local prevalence of the latter disease and the occasional conjunction of the two conditions in the same subject afford some ground for the opinion which I have formed that the one is merely a different phase of the other; that the callosity, in fact, is due to a horny degeneration or atrophy of a patch of mycetoma. Additional weight is lent to this view by the fact that the history is frequently the same. The patient often dates both undoubted oma and callosities to a prick of a thorn. The photograph (Plate 1) shows a case in which there were many callosities on the soles h feet; Plate 1, fig. 2, the two conditions occurring side by side in ıme foot; and Plate I, fig. 3, a distinct patch of mycetoma with er internal to it which, I think, is progressing toward a condition ·ny degeneration. As regards the disease shown by Plate II, fig. 4, ıot wish to discuss the point; it represents a condition which I have observed before, and I should be very glad if light could be thrown it.

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[1] Read at the first meeting of the Far Eastern Association of Tropical Medicine, held at Manila March 12, 1910.

[2] Major, I. M. S., Rajkot, Kathiawar, India; delegate from the government of India.

other stage of the disease, the existence of which has been denied by authorities, is shown in Plate II, figs. 5 and 6. I am aware that lary deposits in the lymphatic glands have been previously reported, hese are the only two cases which I have personally seen. In this mycetoma would appear to be as dangerous as and more rapid in read than some varieties of carcinoma; but fortunately such a opment is very rare. Recurrence at the site of amputation is ently even more rare, and I have only once seen a case in point; is the growth recurred in the flop after a Syme's amputation. My experience in all cases where there seems to be any reasonable prosof extirpating the fungus in that way leads me to excise the growth, eference to sacrificing the foot, even though it may be impossible ow a very liberal margin of sound tissue. The results of treatment atisfactory in ordinary cases, and in the malignant type probably amputation would fail.

the 26 patients above referred to, 18 were males, and 13 cultivators cupation. Fifteen of the growths discharged black granules and 11 w granules.

ILLUSTRATIONS.

PLATE I.

FIG. 1. *Showing callosities.*

Male, 38, Hindu, cultivator. Says the corns first began to appear two years ago. He attributes the condition to injury by thorns, which, he says, was succeeded by induration of the skin. Distinct callosities are visible in the photograph, and it will be noticed that they do not all correspond to the areas most subject to pressure, as in the case of ordinary corns.

FIG. 2. *Showing mycetoma with callosities.*

Another specimen is available, which shows this combination equally well, but is not figured. Male, 20, Hindu, cultivator. He states that a year ago, while working in the fields, a thorn entered his right foot, at the base of the second and third toes. An abscess formed, and subsequently a hard, brawny swelling, which later burst and discharged black granules. The photograph shows an undoubted mycetoma, discharging black granules, in the situation indicated above; and several callosities, resembling those of fig. 1, can be seen scattered over the sole of the foot.

FIG. 3. *Showing mycetoma, with an adjacent patch, apparently mycetoma degenerating into a callosity.*

Male, 33, Hindu, corn and general dealer. He states that about a year ago a hard swelling appeared about the middle of the outer border of the right foot, which ultimately broke down and discharged black granules. Shortly before the swelling was noticed he had struck his foot against a stone, and he attributes the disease to that injury. In the photograph an undoubted mycetoma can be seen, which discharged black granules. Internal to this is an indurated patch, which was apparently mycetoma undergoing indurative changes, and which probably (it is suggested), if left alone, would have developed into a callosity like those seen most typically in fig. 1.

PLATE II.

FIG. 4. *Showing a diffuse induration of the sole of the foot, possibly a degenerative phase of mycetoma.*

Male, 20, Hindu, clerk. He states that about five years ago he noticed a small corn (*kapasi*) at the middle of the sole of the right foot. This was followed by others, and gradually the greater part of the sole became covered with a horny growth. No discharge, granular or otherwise, was ever noticed.

On excision, the growth was sent to the Imperial Research Institute, Kasauli, for examination. The report received stated that the microscopic appearances were those of a chronic granuloma, resembling mycetoma, but that no mycelial elements could be discovered.

HOOTON.

FIG. 5. *Mycetoma, showing secondary deposits in inguinal glands.*

e, 40, Hindu, no occupation. She states that about a year ago she first ced "corns" on the sole of the right foot, which she at first tried to remove. lling appeared at the groin shortly after the commencement of the disease he foot. The photograph shows a well-marked mycetoma, which discharged ow granules, and there are three sinuses in the groin, in the pus from ch similar granules appear.

FIG. 6. *Mycetoma, showing secondary deposits in the inguinal glands.*

35, Hindu, cultivator. He dates the commencement of the disease from the k of a thorn in the sole about three years ago, and states that in this and er places "corns" formed. The first swelling in the groin is stated to have eared three months after the first symptoms. The photograph shows a well-ked mycetoma of the right foot, with a similar growth spreading upwards downwards from the groin into the abdomen and thigh. Yellow granules discharged from sinuses in both situations.

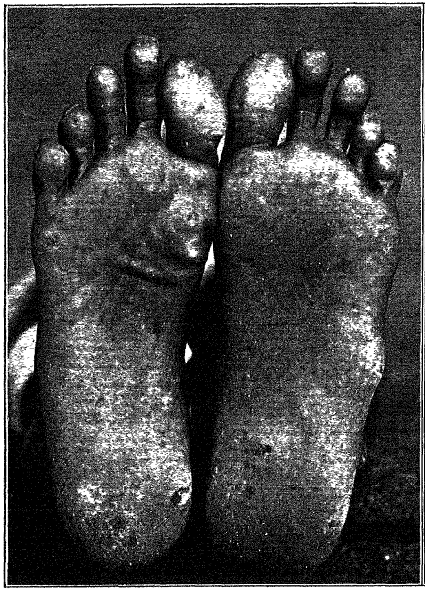

FIG. 1.

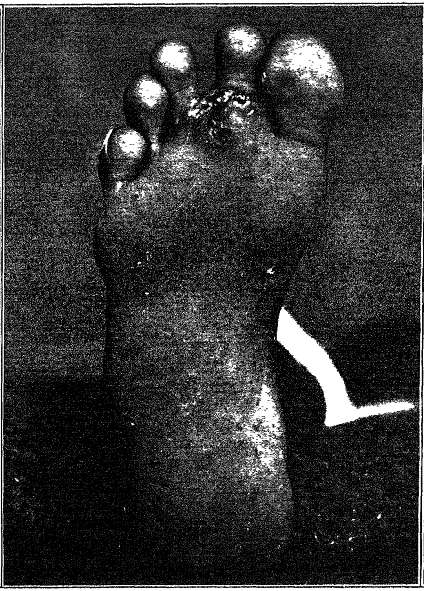

FIG. 2.

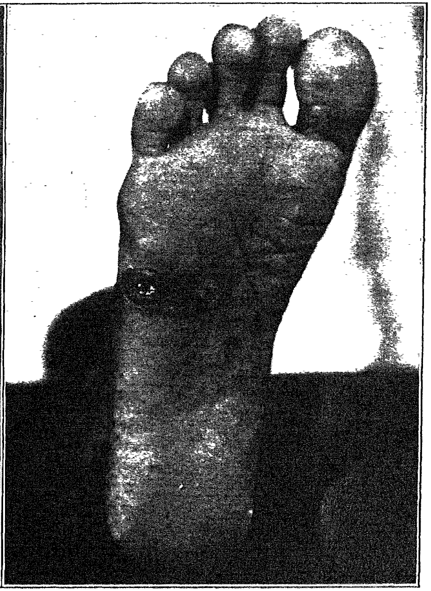

FIG. 3.

PLATE I.

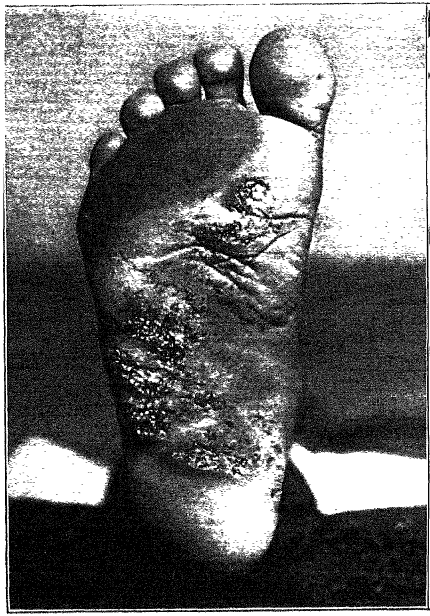

FIG. 4.

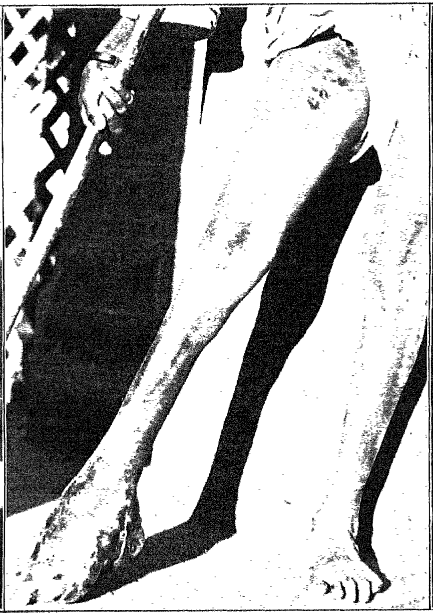

FIG. 5.

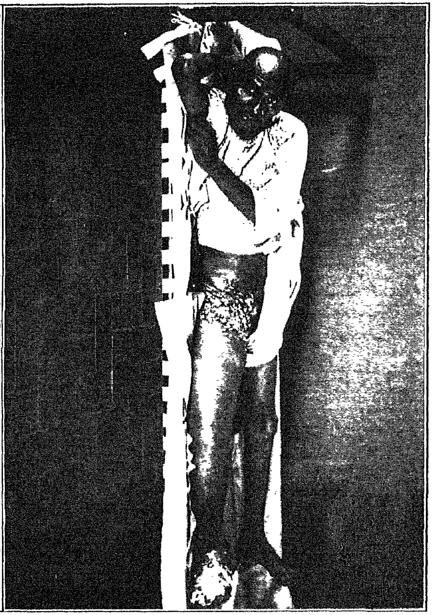

FIG. 6.

PLATE II.

THE PREVENTION AND TREATMENT OF AMŒBIC ABSCESS OF THE LIVER.[1]

By Leonard Rogers.[2]

During the last few years much progress has been made in our knowledge of the pathology of tropical liver abscess, in which the workers in the Philippine Islands have played a noteworthy part. Nevertheless, I venture to hope that, owing to the abundance of opportunities for investigating this subject in Calcutta, my experience of the last ten years' work there may not be without interest, more esvecially with regard to the practical points of the prevention and treatment of the disease based on advancing knowledge regarding its etiology.

RELATIONSHIP OF TROPICAL LIVER ABSCESS TO AMŒBIC DYSENTERY.

As recently as 1902, the opener of a debate on dysentery at the British Medical Association[3] maintained that tropical liver abscess was not closely related to dysentery. At the same meeting I brought forward the results of investigations in Calcutta on this point, in a series of cases in which both clinical histories and post-mortem records were available, with the following results:

Relationship of dysentery to tropical liver abscess.

	Total.	Per cent.		
Clinical and post-mortem evidence of dysentery	35	55.5	76.18	90.48
No history, but post-mortem evidence of dysentery	13	20.63		
History, but no post-mortem evidence of dysentery	9	14.3		
No history or post-mortem evidence of dysentery	6			9.52

The above cases include a number of old records dating back to 1872, when the relationship of the two diseases was less well known, so dysentery may not always have been sought for and recorded. If we take the more recent post-mortem records of the last ten years, a considerable majority of which have been performed by me, we obtain the following figures.

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[1] Received for the first biennial meeting of the Far Eastern Association of Tropical Medicine, held at Manila March 5–14, 1910, after the close of the sessions.

[2] Professor of pathology, Medical College, Calcutta.

[3] *Brit. Med. Journ.* (1902), 2, 841.

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Bowel condition in fatal cases of liver abscess.

	Total.	Per cent.
Amœbic dysentery present	35	77.8
Scars of old dysentery present	9	20.0
No evidence of former dysentery	1	2.2

Evidence of dysentery, always of the amœbic type, is thus seen to be almost constantly found after death from amœbic abscess of the liver, while the few exceptions can readily be explained on the assumption that a mild latent infection had completely healed before death from the hepatic complication, leaving no very evident scarring behind.

Once more, an analysis of the excellent clinical notes on liver obscess treated in the European General Hospital at Calcutta during the last nine years has furnished the following data:

		Total.		Per cent.	
Dysentery	In hospital	18	36	72	86
	Within 3 months	10			
	Over 3 months ago	8			
Diarrhœa only			7	14	
No diarrhœa			7	14	

There was thus a history of dysentery or diarrhœa in 86 per cent of the cases of liver abscess, while we have already seen that these symptoms may be absent even when amœbic ulceration of the large bowel, commonly limited to the cæcum and ascending colon, are actually found postmortem.

A further study of the cases in the Medical College Hospital demonstrated that in at least 80 per cent the symptoms of dysentery had preceded the formation of liver abscess, while when the bowel symptoms supervened after signs of acute hepatitis, it is doubtless only a recrudescence of old intestinal trouble.

For these various reasons I hold that amœbic dysentery, either active or latent, invariably precedes amœbic hepatitis, which is secondary to it by infection through the portal system. In 1903 [4] I demonstrated that the earliest minute amœbic multiple abscesses of the liver commence in the terminal branches of the portal veins, and I have several times since found similar small multiple abscesses of the liver containing amœbæ, but no bacteria or cocci.

THE PRESUPPURATIVE STAGE OF AMŒBIC HEPATITIS.

The vast majority of patients coming to hospital with an abscess of the liver give a history of fever, with or without pain in the hepatic region, lasting for several weeks and not rarely for several months. They have usually been given quinine and other drugs without avail, the true nature of the disease only becoming apparent with an increased prominence of the localized symptoms. When examining the blood of a large number of consecutive fever cases in the Calcutta European Hospital, I realized that the fever of the presuppurative stage of amœbic hepatitis could almost invariably be recognized by the occurrence of a leucocytosis, usually with no marked increase in the proportion of the polynuclears. I had previously come to the conclusion that active or latent amœbic ulceration of the large bowel always preceded liver complication, and that ipecacuanha is of great value in amœbic dysentery, a point in which Indian experience is at variance with the general opinion in the Philippine Islands, although Simon in New York and Dock in New Orleans are now converts to the view which Sir Patrick Manson and the writer have long advocated. It was but a simple step forward to try the effect of full doses of ipecacuanha in the early stages of amœbic hepatitis, with a view to curing the exciting cause, namely, the ulcers in the large intestine, as had indeed been done empirically many years before by Maclean and Norman Chevers, although with the increasing vogue of the saline treatment in dysentery the use of ipecacuanha had fallen largely out of favor even in the latter disease and had been almost entirely neglected in hepatitis of recent years. I have already published several papers[5] illustrating the marvellous effects of this drug in preventing acute hepatitis passing on to liver abscess, sanctioned even when experienced surgeons were convinced that suppuration had already taken place. A consecutive series will be found in my work on Fevers in the Tropics, while I now have notes of several scores of equally striking cases, which it is unnecessary to relate. It will suffice here to say that during the last four years no patient has developed an amœbic liver abscess under treatment for hepatitis in the 100 beds for males in the Calcutta open wards of the Calcutta European Hospital, although this was formerly a frequent occurrence, while the number of patients admitted with an abscess of the liver has also fallen considerably. Even more striking evidence of the value of this plan is furnished by the returns of the British army in India, for during the two years which followed the publication of my first series of cases the mortality from liver abscess in English troops in India has fallen by 60 per cent, although stationary for the previous thirteen years. With the wider adoption of this treatment in the earliest stages of tropical hepatitis, I feel sure even better results will be obtained in the army, as the patients come under skilled medical observation at the beginning of their illnesses. It is already abundantly clear that I did not exaggerate when I wrote that amœbic or tropical liver abscess is an easily preventable disease in the great majority of instances, and the occurrence of amœbic suppuration in the liver should cause serious questions in the mind of the medical man in whose hands it has been allowed to develop.

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[4] *Ibid.* (1903), 1, 706.

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[5] *The Therap. Gaz.* (1909).

Diagnosis.—Now that I have shown that leucocytosis of a marked degree occurs in the readily curable presuppurative stage of amœbic hepatitis, it is clear that we can obtain no aid from an increase of the leucocytes as a sign of the actual formation of an abscess in the liver in a doubtful case. Complete fixation of the diaphragm and rarely an increased density of the liver shadow, as seen with the X rays, may be present in cases which clear up under ipecacuanha. I have also seen a local swelling in the epigastrium and even œdema over the ribs in cases rapidly cured in this way. In fact, I know of no certain symptom of the formation of pus within the liver except a fluctuating swelling in the hepatic region. It is for this reason that exploratory puncture is so often performed in acute hepatitis for the confirmation of suspected liver abscess, only too often with a negative result; nor is this operation the harmless procedure it is frequently represented to be. I know of several fatalities from hæmorrhage into the abdominal cavity resulting from it, while Lieutenant-Colonel Hatch, I. M. S.,[6] has done a public service by having had the courage to publish a series of six such cases in his experience, occurring in the Bombay Presidency. Moreover, this disaster is most likely to occur in cases in which no abscess is found, in some of which it was proved post-mortem that no pus had formed in the liver. It is especially in the acutely congestive presuppurative stage that serious bleeding follows exploratory puncture of the liver; yet it is often most important to detect and deal with an abscess in the liver before it has clearly revealed itself by its large size or through implicating surrounding organs, and hitherto the needle was the only means of deciding if suppuration had taken place or not. Fortunately, we are now in possession of a much simpler and safer plan, for if the disease is still in the presuppurative stage the fever, pain, and liver enlargement all rapidly yield to ipecacuanha, which is as much a specific for amœbic hepatitis in the early stage as quinine is for malaria. No harm results from a few days' delay if pus has already formed, while the danger of further abscess formation will be greatly reduced by the drug treatment. If, however, fever continues for a week or more without material diminution, and especially if the local pain remains, an abscess has probably already formed and exploratory puncture may now be performed with much less risk, as the general congestion of the liver will have been greatly lessened by the ipecacuanha. Since this rule has been followed in the Calcutta European Hospital negative exploratory punctures for liver abscess have become as rare as formerly they were frequent. In the Medical College Hospital explorations are still performed by the surgeons in doubtful cases, without a previous trial of ipecacuanha, and negative results are still obtained in cases which subsequently recover completely on ipecacuanha.

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[6] *Indian Med. Gaz.* (1898).

THE STERILITY AS REGARDS BACTERIA OF AMŒBIC ABSCESSES OF THE LIVER.

The most important point in regard to treatment is the absence of bacteria from the pus of amœbic abscesses of the liver in the great majority of cases. In the first series in which I examined the pus obtained at the time of the operation, I found two-thirds to be sterile, but this was an underestimate, as the aspiration bottles were not always free from bacteria. In a recent series, in which the pus was received direct from the aspirating canula into a sterile test tube, no less than 75 out of 87 consecutive cases, or 86 per cent, were free from bacteria both microscopically and on culture. However, in a few cases very numerous cocci and bacteria are found, occasionally including streptococci. Such cases have a worse prognosis than abscesses containing only the amœba. The great majority, however, of tropical liver abscesses are solely due to the protozoäl organism.

THE FREQUENCY OF BACTERIAL INFECTION AFTER THE OPEN OPERATION FOR PRIMARILY STERILE AMŒBIC ABSCESSES.

When examining pus from opened liver abscesses for amœba, I observed that bacteria and cocci were almost invariably present. I therefore made cultures in a series of cases from the pus obtained in sterile test tubes at the time of opening and again a few days later. In a large number of observations made during the last two years at the Medical College Hospital at Calcutta in no single case did a primarily sterile abscess remain free from infection for as long as three days after being opened and drained in the ordinary way; nor is this surprising when we remember that the sterile, blood-serum-like contents form an ideal culture medium for the organisms, which must inevitably enter from the air at the operation and on subsequent dressings, apart from the frequency with which the copious discharges soak through the coverings, and thus allow of contamination. The organisms will commonly be of but slight virulence, but suffice greatly to prolong the period of exhausting discharges and retard the healing of the wound. In support of this contention it may be well to quote the following remarks of Maj. G. C. Spencer, R. A. M. C., professor of military surgery, Royal Army Medical Colege.[7] Regarding the high mortality of the open operation he writes:

> The chief cause of this high mortality, apart from the presence of more than one abscess, or extreme debility of the patient before operation, is undoubtedly infection of the abscess cavity by pyogenic organisms through the open wound. This is extremely difficult to prevent, no matter how much care is taken. . . .

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[7] *Journ. Roy. Army Med. Corps* (1909).

The great majority of amœbic abscesses are sterile when first opened, and every surgeon with Indian experience is familiar with the usual course of fatal cases. The patient does well for the first few days after operation, then infection occurs, the temperature goes up again, and death from septic poisoning slowly but surely follows.

THE TREATMENT OF A STERILE AMŒBIC ABSCESS OF THE LIVER BY REPEATED ASPIRATIONS AND INJECTIONS OF QUININE INTO THE CAVITY WITHOUT DRAINAGE.

In abscesses due to the ordinary pyogenic bacteria there is no difference of opinion as to the necessity of early opening and drainage. A similar line of treatment in large, cold tubercular abscesses, however, has sometimes been followed by a disastrous secondary infection. Tropical abscesses of the liver for many years past have been almost universally treated by free incision and open drainage, exactly as in ordinary septic abscesses due to bacteria. The results can not be said to be brilliant, for in the Calcutta hospitals the mortality among several hundred cases, treated by very experienced surgeons during the past thirteen years, has been 60 per cent. Now that we know that this form of abscess is caused by a protozoäl organism, and the vast majority of them are free from bacteria when first opened, although infection almost invariably follows their free incision, it is worth considering if some simpler and safer method of treating the disease can not be found. On ascertaining that tropical liver abscesses always contain amœbæ and are usually primarily sterile, I set to work to test the effect of drugs on the causative protozoa in the walls of liver abscesses, post-mortem, and in 1902 recorded the fact that a 1 to 500 solution of quinine would readily destroy the amœbæ under these conditions. I therefore suggested the treatment of bacterially sterile liver abscesses by withdrawal of as much pus as possible through an aspirating needle and the injection of 1.30 grams (2 grains) of quinine in solution into the cavity, no incision or drainage being used. In 1906 I reported with Capt. R. P. Wilson, I. M. S.,[8] two cases successfully treated by this plan, since which several surgeons have recorded similar results. Major Spencer early in 1909 published several, in one of which three aspirations and injections were necessary, while in the other two a single operation sufficed, and he advised the adoption of my plan in all cases, as even if it fails no harm is done, and the patient may be in a better condition to stand the more serious open operation.

During the past year Maj. F. O'Kinealy and C. R. Stevens have kindly given my method a prolonged trial at the Calcutta Medical College Hospital with most encouraging results. The latter surgeon will shortly publish his own conclusions, so I will only here tabulate the results of the cases I have been able to watch in the several Calcutta hospitals during the last few years.

[8] Brit. Med. Journ. (1906) 1, 1397.

Summary of cases treated by aspiration and quinine injection only.

		Abscess cured.	Abscess fatal.
Abscess not opened	Cured	16	
	Abscess cured, died later of dysentery	1	
	Abscess cured, died later of pneumonia	1	
	Died of liver abscess		3
Abscess opened later	Cured	3	
	Died		3
Total		21	6
Abscess evacuated through the thoracic wall			25
Abscess evacuated through the abdominal wall			2

The site of the evacuation of the pus is important, because I find that the mortality of cases treated by the open operation is but 40 per cent when the incision is through the abdominal wall, but no less than 73 per cent when it is through the thoracic wall. The death rate was but 12 per cent in abscesses of the left lobe opened through the epigastrium, owing to their being readily recognized and dealt with while still small. In the above series the death rate among 25 cases evacuated through the chest wall was 24 per cent, or just one-third of the mortality of similar cases treated by the open operation. The three cases in which a fatal result occurred after aspiration and quinine injection alone all had large abscesses, the patients being nearly moribund, and the open operation would almost inevitably have been rapidly fatal. On the other hand, several abscesses containing from 1.5 to 3 liters (3 to 6 pints) of pus were successfully dealt with by my plan, including some in which it was considered that the open operation would have given little or no chance of recovery, one containing 3.3 liters (112 ounces) of pus. In one case the patient died of dysentery three and one-half months after cure of the liver abscess, my suggestion to give ipecacuanha at the time the abscess was first aspirated not having been adopted. In another case no less than 2.5 liters (86 ounces) of pus were aspirated at the first operation, nine days later 532 cubic centimeters (18 ounces) were obtained and seven days later still only 300 cubic centimeters (10 ounces) were evacuated, quinine being injected at each aspiration. After another eight days only 150 cubic centimeters (5 ounces) of thin bile, without pus, were withdrawn, so no quinine was injected. A few days later the patient died unexpectedly and at post-mortem, left apical pneumococcal consolidation of the lung was found, quite independently of the hepatic trouble. The liver abscess was found to have contracted so as to hold only 75 cubic centimeters (2½ ounces) of thin bile with no pus or amœbæ, the contents being sterile, as they had been throughout. The fibrous wall was smooth and nearly half an inch in thickness, encystment having taken place. The patient had been given a course of ipecacuanha, and the cæcum showed scars of recently healed ulcers, together with a few depressed slits of those almost healed. Another remarkable case was one of Major O'Kinealy's, in which no less than 3 liters (6 pints) of pus were aspirated from the liver of an Indian patient. This pus was found to be sterile as regards bacteria. Five days later 1,064 cubic centimeters (36 ounces) were withdrawn, and 2.66 grams (40 grains) of the soluble bihydrochloride of quinine injected. The patient improved steadily and put on 8½ kilograms (18½ pounds) weight in five weeks, recovering completely. Such cases speak for themselves.

In carrying out this method, the skin at the seat of puncture must be thoroughly sterilized to prevent bacteria being carried into the abscess cavity. The T tube of the exhaust bottle should have a large caliber to allow thick pus to pass, the cavity being emptied as far as possible, and some of the pus put in a sterile test tube for bacteriological examination. A previously boiled solution of the bihydrocholoride of quinine, 2 grams to 100 cubic centimeters (10 grains to the ounce) is next injected into the cavity through the canula, which is then withdrawn and collodion applied externally. If only a few cubic centimeters (ounces) of pus have been found, 60 cubic centimeters (2 ounces) of the quinine solution will suffice, but if a pint or more of pus has been removed, 120 cubic centimeters (4 ounces) should be injected. In some cases the temperature at once falls and all the symptoms rapidly subside, but more frequently the process has to be repeated after a week, while third and fourth aspirations are sometimes required in large abscesses. If a previously present leucocytosis completely subsides, little or no pus is usually obtained at a second operation, but the continued presence of leucocytosis is an indication for further aspirations, quinine being injected each time. In Major Spencer's cases the hydrobromide of quinine was used successfully. In the rare cases in which the aspirated pus is found to be swarming with bacteria the abscess must be opened. Further experience is required to lay down the exact indications for this method, but the success already obtained is sufficient to make it advisable to give the patient the benefit of a trial of this simple and safe mode of treatment in all cases in which there is no definite contraindication before resorting to the much more serious open operation.

STERILE SYPHON DRAINAGE OF LIVER ABSCESS.

The practical impossibility of maintaining sterility in the Tropics after the open operation for liver abscess, taken with the occasional failure of my plan of aspiration and quinine injecton, suggested to me the advisability of devising a method of sterile drainage, combined with quinine irrigations. For this purpose I got Messrs. Down Brothers, of London, to make for me the flexible sheathed trocar.[9] It is made in various sizes and can be used as an aspiration trocar, the abscess being first located with the ordinary small-sized trocar if its position is not accurately known. After the cavity is evacuated a piece of tubing of large bore is connected with the end of the flexible sheath, and carried into a bottle of antiseptic lotion under the bed, siphon drainage being thus established. The sheath is so flexible that it can safely be left in the cavity and used as a drainage tube. By means of a Y-shaped silver tube connected with pressure tubing the aspirator can be applied daily to the flexible sheath, and any thick pus which is not draining can thus be withdrawn. Through the other limb of the Y tube, with a sterile glass syringe, sterile quinine solution is injected daily, to kill the amœbæ in the wall of the abscess. The discharge rapidly lessens and the cavity contracts. Thus, in the first case in which this method was used in Calcutta by Capt. J. G. Murray, I. M. S.,[10] in less than a week a cavity originally containing about 500 cubic centimeters (1 pint) of pus would admit only 15 grams (one-half ounce) of the quinine solution. After two weeks (an unnecessarily long time, to be on the safe side) the canula was withdrawn, leaving a 10 centimeters (4-inch) sinus. In three days the sinus had healed up to the surface with only a few drops of serous discharge, and in a week from the removal of the canula the skin had healed over and the patient left the hospital, striking contrast to the slow process attending infected liver abscess wounds after the open operation. The patient was discharged from the hospital in less than half the time that any similar liver abscess evacuated through the chest wall had been cured by the open operation in the European Hospital during the last nine years. The great advantages of sterile siphon drainage combined with sterile daily quinine irrigations is thus clearly established, but the marked success of repeated aspirations and quinine injections recently obtained promises greatly to limit the necessity for the employment of my flexible sheathed trocar.

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[9] *Ibid.* (1908), 2, 1246.

THE USE OF IPECACUANHA IN THE AFTER-TREATMENT OF AMŒBIC LIVER ABSCESS.

Lastly, I would urge that every patient operated on for amœbic liver abscess should be given a course of full doses of ipecacuanha as soon as possible, with the view to healing the ulcers in the large bowel, which have originated the hepatic trouble and are often latent and give rise to no symptoms. This will greatly lessen, or entirely prevent, the formation of further liver abscesses, the occurrence of which, during the convalescence after operation for a collection of pus, is one of the most trying complications the surgeon in the Tropics is liable to meet with. If the operation is resorted to, the cavity should also be washed out with sterile quinine lotion daily, as this will rapidly lessen the discharge if no serious bacterial infection has resulted. As an example of the value of this meausure, I may mention the case of an European who had been submitted to four operations for liver abscesses in as many months and was still suffering from severe pain and high fever, being in a very precarious condition. He was at length put on ipecacuanha, and quinine irrigation was adopted. The next day his pain had almost gone, the temperature rapidly fell, and he began to recover from that time, although several weeks were required for the healing of his extensive wounds. I have seen him in very good health a year after leaving the hospital, and he has recently passed a medical examination for employment as an engineér on a large railway. He was so impressed with the immediate relief afforded to him by the ipecacuanha that he continued to take it daily for a year after his recovery. In fact, I attribute not a little of the recent improvement in the results of the treatment of liver abscess in the Calcutta hospitals to the adoption of a routine course of ipecacuanha in the after-treatment of liver abscesses, however they may be dealt with.

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[10] *Loc. cit.*, 1330.

INTESTINAL AMOEBIASIS WITHOUT DIARRHOEA.

A STUDY OF FIFTY FATAL CASES.

By W. E. Musgrave.

(From the Biological Laboratory, Bureau of Science, Manila, P. I., and the Department of Clinical Medicine, Philippine Medical School.)

Notwithstanding the fact that such careful and experienced observers as Osler, Dock, Councilman, Laffleur, Kartulis, Tuttle, and many others have mentioned the absence of diarrhœa in certain severe and even fatal cases of amœbic infection of the colon, the fact does not appear to have received the general recognition which its importance deserves.

In 1904 Musgrave and Clegg again called attention to this condition, having in several articles which have appeared since that time, reported cases and emphasized its occurrence. The purpose of the present paper is not to establish a new fact, but to show that the prevalence of amœbic infection of the colon without diarrhœa is of sufficiently frequent occurrence to deserve careful consideration by clinicians and to make evident the necessity of altering our conception of the disease to conform with the acceptance of such observations.

In selecting the 50 cases for this report, only those in which the clinical observations were of sufficient accuracy for publication and in which the diagnosis was confirmed by autopsy have been used. Of the 50 cases, 8 were foreigners and 42 natives of the Philippine Islands, 47 were males and 3 females. The causes of death were as follows:

Three from peritonitis following perforation of the appendix—two of these produced by amœbic ulceration, the other by an unknown cause, not amœbic.

Four from liver abscesses—one perforating into the right pleura, one into the abdominal cavity, and two were without perforation.

One from acute pericarditis.

Eight from pulmonary tuberculosis, and in three of these abdominal tuberculosis was also present.

Two from chronic æstivo-autumnal fever.

Five from perforation of amœbic ulcers in the large intestine—four times in the cæcum and ascending colon and once in the transverse colon.

Seven from acute beriberi.

Twenty from lobar pneumonia.

Many more could be added to this group of cases in which diarrhœa developed only a few days before death, and then this symptom was often due to intercurrent disease, such as cholera, which caused the exitus. Still another group which might well be classed here includes those patients in which diarrhœa or clinical dysentery developed a few days before death and in which, at autopsy, *advanced* amœbic lesions were found. However, as these cases did show some symptoms of diarrhœa, they are not here considered. In the 50 instances which form the subject of this paper, looseness of the bowels, except from cathartic medicine, was not at any time a symptom. Indeed, in several constipation was a noticeable and constant feature of the disease up to the time of death.

Pathology.—Characteristic amœbic lesions were present at autopsy in all of the 50 cases. These lesions varied in type from those which were just beginning to those showing ulcers having the characteristic extensive destruction of the mucous membrane of the bowel so often seen in cases of amœbiasis of long standing. The lesions were distributed as follows:

Not recorded, 5 cases; confined to cæcum and ascending colon (including 3 of the appendix), 27; entire large bowel (except sigmoid and rectum), 9; rectum, 0; descending colon and sigmoid flexure (alone), 2; transverse colon (including splenic flexure), 2; cæcum, hepatic and splenic flexures, 5.

Other parasites, such as monads, trichuris, hookworms and ascaris were present in several of these patients; the lesions of other diseases have been mentioned above. The duration of the infection, judging from the autopsy findings, varied, but in most instances the lesions indicated processes of long standing.

Symptoms.—The occurrence of general symptoms in these patients varied considerably, and if we except those due to the intercurrent disease were *entirely absent* in some of them. In others there were present one or more clinical manifestations which I have described elsewhere as occurring in latent and masked types of amœbic dysentery. While none of these symptoms may be said to be pathognomonic of amœbic infection, yet when several are present in the same patient, in the absence of any other satisfactory cause, they are strongly suggestive of amœbic infection, especially in zones where this disease is endemic.

Abdominal "aching," usually more or less general, worse at night and early in the morning, and often accompanied by flatulence and occasionally by constipation, is one of the most frequent of the symptoms, but unfortunately this is extremely common among a large class of patients with mild forms of indigestion who are not suffering from amœbic infection. Distension of the abdomen and the discomforts of flatulence are of frequent occurrence. Constipation is a particularly common complaint. In this class of patients the lack of result from ordinary doses of the usual cathartics may be brought to the attention of the physician, or in other instances the action of these drugs may be unusually severe and prolonged. Loss of weight occasionally becomes a noticeable symptom, but in many instances the nutrition remains good and the patients may even increase in weight. Interference with the appetite is usually first shown by lack of desire for breakfast and this may be accompanied by morning nausea and the accumulation of considerable mucus in the mouth and throat during the night. Active indigestion or dyspepsia are not very common symptoms, but do occur in a certain percentage of the cases.

Excessive perspiration, particularly of the palmar and plantar surfaces, is very frequent, and in many instances the physician is first consulted because of this complaint. The whole chain of symptoms of so-called "Philippinitis" or tropical neurasthenia, characterized by dullness, headache, loss of memory, weakness, desire for sleep, etc., is a rather common condition encountered in these infections, but it is also particularly prevalent in the absence of such parasitic invasion.

Diagnosis.—When we come to study the clinical phenomena shown by this class of cases, it is seen that there is nothing specific or definite in any one, or in all the findings, except the one of the presence of amœbæ in the stools. The patients are of the class sometimes reported as "healthy people with amœbæ in the stools," and, as alluded to in one of my previous papers, it is erroneous to report all of such cases as being healthy or as those "suffering from diseases other than dysentery."

This brings us to the important point which of itself is sufficient excuse for this paper, namely, How are we to diagnose amœbic infection of the bowel during life? Ten years' continuous experience with this disease clinically, in the laboratory and at autopsy, has convinced me that its diagnosis is not possible except through information secured by a microscopic examination of the fæces. Looseness of the bowels in the form of dysentery or diarrhœa has long been the strong diagnostic point, but the facts show it also to be a very unreliable one.

The sygmoidoscope gives valuable and positive evidence of infection in patients with ulceration in the lower part of the bowel, but does not furnish aid in the large percentage of early infections in which the lesions are above the range of this instrument. As a result of careful application of all known diagnostic methods in the infection we have but one constant finding, and that is the presence of amœbæ in the bowel discharge. The question whether the presence of amœbæ in the stools of patients should be considered sufficient evidence of infection for the institution of treatment is still a disputed one. A number of authors agree with the late Professor Schaudinn that there are two easily differentiated species of amœbæ encountered in stools, one a pathogenic parasite and the other a harmless commensal.

I have already discussed this subject fully in other publications.

A QUICK, SIMPLE, AND ACCURATE METHOD OF MAKING DIFFERENTIAL BLOOD COUNTS IN WET PREPARATIONS AND ITS ADVANTAGES IN THE DIAGNOSIS OF SURGICAL AND TROPICAL DISEASES.[1]

By E. R. Stitt.[2]

(From the United States Naval Hospital, Cañacao, P. I.)

In the diagnosis of acute abdominal conditions and almost to an equal extent in other surgical affections, the leucocyte count has the confidence of the surgeon. The same would obtain for the polymorphonuclear percentage were it not for the errors incident to the usual method of making differential counts. A smear equally distributed, a satisfactory stain and good technique are necessary for results that will give true findings. These three factors do not always go together, as any experienced laboratory worker will admit, and for the average man they rarely obtain. Again, almost any variation in the leucocyte percentages can be obtained in the usual easily prepared smear made with some form of spreader on a slide. To make this evident it is only necessary to refer to the usual method of ploughing out the polymorphonuclears to the margins, a method used in preparing smears for determining the opsonic index. I was told by one of our leading American laboratory workers that it was necessary for him to discard several thousand smears of yellow-fever blood, made for the purpose of studying leucocytic percentages in the disease, for the reason just stated.

It has been my experience that the only method of making films which gives fairly accurate findings is that of Ehrlich—the sliding apart of two cover glasses between which the drop of blood has distributed itself in a thin layer. Even with this procedure we meet sources of error such as the difficulty of distinguishing polymorphonuclears from transitionals in those portions of the smear which fail to show a single layer of red cells and in particular by reason of the large number of disrupted cells which are peculiarly common to pathologic blood and which show themselves in the form of more or less uniformly stained blotches, the former leucocytic character of which can not be determined. By checking the percentages obtained by the method I shall describe and those secured by the usual means, I have found that in septic conditions these disrupted cells are largely polymorphonuclear, while in such conditions as malaria and dengue they are chiefly transitionals.

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held at Manila March 12, 1910.

[2] Surgeon, United States Navy.

The surgeon of the present day always demands a leucocyte count, and the medical man in the Tropics finds it almost equally necessary in differentiating diseases which show a leucocytosis from those which present a leucopenia. Consequently, a distinct saving of time would result if it were possible to obtain other findings in the same preparation used for ascertaining the number of leucocytes per cubic millimeter.

By employing the ordinary technique for making a count of the white blood cells, with the exception that I use a diluting fluid made by adding five drops of Giemsa's stain to 5 cubic centimeters of 2 per cent formalin, I also am able quickly and, I am convinced, accurately to make a polymorphonuclear percentage count, or a complete differential count in addition to that of the leucocytes.

Another advantage is that blood parasites are also perfectly stained, are shown distinctly, and by reason of the larger amount of blood visible in each field, the finding of them is far less tedious than where a stained, dry film is used.

In preparing the Giemsa stain I use the original method by dissolving 0.08 gram Azur II and 0.3 gram Azur II eosin in 25 cubic centimeters of glycerine at 60°C., then adding 25 cubic centimeters of methyl alcohol, allowing the whole to stand overnight and then filtering.

The ordinary commercial formalin and distilled water are used in preparing the 2 per cent formalin solution.

Better results are obtained when the Giemsa solution is added to the formalin just prior to using. The staining power of the mixed formalin and Giemsa begins to diminish after a few hours, therefore it is better to drop the Giemsa solution from a dropping bottle into the formalin in a watch glass at about the time the blood count is to be made. The best results are secured when the mixing in the pipette bulb is done immediately after taking up the blood and diluent.

The usual technique in making the hæmocytometer preparation is employed, a Türck ruling being used. I count the leucocytes in the 3 upper or lower square millimeters, divide by 3 to obtain an average per square millimeter, multiply by 10 for the content of a cubic millimeter and then by 20 for the dilution. (Blood to 0.5, diluent to 11.) This can be done mentally and requires no calculation on paper. Having counted the leucocytes I again go over the same portion of the ruled surface and determine the polymorphonuclears and estimate the percentage of these to the total leucocytes.

It is unnecessary in such counts to have an assistant record the results. Of course, in making a complete differential count it is preferable to have some one tabulate them, or laboriously to do this personally.

The red cells are practically diaphanous and not disintegrated as they are when acetic acid is used as a diluent: consequently it is easy to distinguish the particulars concerning the size, etc., of a particular red cell containing a malarial parasite. Whether it is possible to determine the species of malarial parasite in such a preparation I am unable to state, as I have had only benign tertian and æstivo-autumnal blood to work with since using this method. At any rate I always make an ordinary Ehrlich smear at the same time I take the blood for the white count, so that I have material for further study with a one-twelfth objective should such further study seem to be advantageous.

My best results have been obtained with a one-sixth objective. Higher powers are of course impracticable by reason of the thickness of the cover glass of the hæmocytometer.

The following are the appearances of the various leucocytes.

Eosinophiles.—In these the bilobed nucleus stains rather faintly and the color is greenish-blue. The eosinophile granules show easily as coarse, brick-dust colored particles.

Polymorphonuclears.—The nucleus stains a deep rich violet-blue, but of a less intense color than of the small lymphocyte. The shape of the nucleus is typically 3 or 4 lobed, but even when of the horseshoe shape of a transitional nucleus, it is easily recognizable by the intensity of the nuclear staining. The distinctness of the cell outlines produced by the fine yellowish granulations in the cytoplasm makes the polymorphonuclears very easy of differentiation.

Small lymphocytes.—The nucleus is perfectly round and stains to a deep rich blue. It is almost impossible to make out any cytoplasmic fringe.

Large lymphocytes.—The nucleus here is round and of a lighter blue than that of the small lymphocyte. The cytoplasm is nongranular and sharply defined from the nucleus.

Large mononuclears.—These show a washed-out, slate-colored nucleus which blends with the gray slate-blue staining of the cytoplasm, so that there is an indefiniteness of outline in the more or less irregularly contoured nucleus.

Transitionals.—These have the same characteristics as the large mononuclears, but with a more faintly stained and more indented nucleus. The large mononuclears and transitionals stand out as slate-colored cells without any sharp nuclear definition. When very much degenerated these cells have a greenish hue.

The young ring forms of malaria show as violet-blue areas in the red cell. When half grown or approaching the merocytic stage the containing red cell takes on a faint pink color, thereby differentiating it from the noninfected red cells. At the same time, the parasite is extruded and has the appearance of a violet-blue body projecting from the margin of the red cell. It is as if a blue body were budding from a pink one. The malarial crescents are brought out with the greatest distinctness.

Trypanosoma lewisi in the blood of rats stains quite distinctly. With the comparatively low powers which it is necessary to use, I have been unable to assure myself of chromatic staining.

DISCUSSION ON THE PAPER, "STUDIES ON INFANT MORTALITY," BY DOCTORS McLAUGHLIN AND ANDREWS.

Dr. H. M. Neeb, medical officer of the first class, delegate from Her Majesty's Government of the Netherlands Indies.—Doctors McLaughlin and Andrews have told us in their interesting paper that convulsions bring about the deaths of many children. I wish to inquire if blood examinations were made with the view of determining whether malarial infection was present. I ask this because in our experience in the Netherlands Indies it not infrequently is true that such an infection in children really is the cause of convulsions and of death.

Dr. W. E. Musgrave, of the Biological Laboratory, Bureau of Science, professor of clinical medicine. Philippine Medical School, Manila, P. I.—Doctors McLaughlin and Andrews are to be congratulated on their contribution to the study of the subject of infant mortality. That part of the paper referring to "infantile beriberi" is particularly interesting, and the pathologic picture described deserves careful study from clinical and etiologic viewpoints. The most important points for discussion are: First, is the described pathologic picture the expression of an etiologic entity? Second, if so, is the etiologic factor that of beriberi?

The chief diagnostic points in the pathology are dilatation and hypertrophy of the right heart, anasarca and congestion of internal viscera, and congestion of the lungs. Most of these findings, as the authors state, may be explained by the condition of the lungs. The described lesions in these latter organs are somewhat similar to those often seen in acute bronchitis in infants, especially when autopsy has been delayed for several hours. Acute respiratory troubles are very common in infants in this country (16 of the authors' series of 219 died of pneumonia), and in the further study of these cases these should be carefully considered, both from the clinical and pathologic side. The anatomic picture of beriberi in the adult is not very characteristic, and in most instances an anatomic diagnosis is possible only by exclusion. Beriberi is, of course, a neuritis and histologic studies always show lesions of the nerves, but even these are not of a proved specific nature. The clinical side of the subject is not fully worked out, and usually probably includes other conditions besides the neuritis. Finally, in spite of the recent brilliant work of Fraser and others on the etiology of the disease, the present status of the beriberi question is indefinite and its etiology is not finally determined. Its position is comparable with that of malaria before Laveran's discovery of the parasite.

In view of this, would it not be better to retain the native names of *suba* or *taon* for the condition described by McLaughlin and Andrews at least until such time as the etiologic agents and clinical picture are made more definite?

The hypothesis that a faulty or disturbed metabolism is the etiologic factor in this group of cases might be open to some criticism, at least in the light of our present knowledge. This is particularly true as to the separation of breast-fed from artificially fed children. Experience in hospital wards and clinics has shown that while practically all Filipino children are fed from the breast, particularly vicious forms of artificial feeding also are at a very early age made to supplement nature's method. Again, it should be mentioned that numerous analyses of mothers' milk taken from the class of people under discussion and analyzed by Bliss, Richmond,[1] Bacon and others of the Bureau of Science have not shown abnormalities in the composition of the milk which would indicate that it is responsible for a sudden acute, fatal disease.

I would also like to call attention to the fact that tuberculosis is extremely prevalent among nursing Filipina mothers.

Dr. Francis Clark, medical officer of health, delegate from the Government of Hongkong.—I believe this to be one of the most interesting papers which has been read. The question of infant mortality frequently arises in the Far East, and at least two-thirds of the natives born die within the first year. The entity described by Doctors McLaughlin and Andrews would suggest the formation of commissions and of systematic inquiries and researches in order further to elucidate the source of infant mortality. Although such commissions have existed, up to the present time they have borne but little fruit. Most careful research has failed to disclose the real causes of death in many instances. I believe the suggestion that many of these deaths are nutritional to be an original one and it opens a new field for research. I believe it to be premature to term this pathologic entity "beriberi." We may regard the disturbances as nutritional without designating them as beriberi. They are perhaps due to nonsufficiency of phosphorus or salts. Doctor Musgrave tells us that in general the milk furnished by the nursing mother is much the same as it is in more temperate countries, but perhaps the content of the milk in salts, and their nature, should be more fully investigated.

Dr. Isaac W. Brewer, Medical Reserve Corps, United States Army.—I have to a certain extent investigated the mortality among infants under one year in the Island of Cebu and have found it to be between 16 and 20 per cent. In that island I found a number of children fed entirely by artificial means. They were given coconut milk, *tuba*,[2] and rice water.

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[1] *This Journal, Sec. B* (1907), 2, 361.

Dr. Ham Aron, professor of physiology, Philippine Medical School.—I have considerable experience in the matter of infant feeding from my connection with the various feeding stations established under my supervision by the Department of Public Instruction, especially in the poorest district of the city, namely, Tondo. My observations have led me to conclude that many of the breast-fed children receive rice or tapioca in addition to mother's milk. I have seen cases of the disease termed beriberi by Doctors McLaughlin and Andrews and which the natives designate as "*taon*." The symptom complex seems to me very closely to resemble the condition which Czerny and the German authors describe as "Mehlnährschaden." I learned that many Filipino children, although breast-fed, in addition are overnourished with the carbohydrates derived from rice or tapioca. The milk of Filipina women is poorer in composition than that of European women. Analyses of individual samples made without regard to the time of day, whether the sample is taken before or after meals, or without taking into account all factors, are of no great importance. However, such as we have show the milk of the Filipina mother apparently to be richer in sugar and poorer in fats and carbohydrates than that of a normal European mother.

I was able to produce in dogs a severe disease by overfeeding them with carbohydrates. The disease is especially characterized by a severe œdema. The clinical picture and the autopsy findings in my experimental dogs in many respects resemble the condition which has been termed beriberi in infants.

Dr. H. Campbell Highet, principal medical officer local government of Bangkok, delegate from His Imperial Majesty's Government of Siam.—The paper which has been read is one of the most interesting which has been given at this session. Only a very minute proportion of the people dying in the East are attended by qualified physicians and hence the usual statistics concerning the causes of death are misleading. A check upon the records is so difficult to obtain, that the work of Doctors McLaughlin and Andrews is of supreme importance. Their results seem to me remarkable in calling attention to the great frequency of infantile beriberi. Whether the condition is true beriberi or not, I am neither prepared to agree to nor to deny. I would prefer to suspend judgment until further work has been done. The pathologic appearances which have been described are certainly those with which we have become very familiar in the cases of adults dead of beriberi, but that breast-fed infants could suffer from beriberi is probably a new fact to most of us. This brings me to the remarkable figures which have been given of the comparative death rate between breast-fed and artificially fed infants. Surely there is a flaw somewhere in the statistics, for the proportion of 70 per cent of deaths in breast-fed infants is totally at variance with that shown us by the history of the world since the days of Adam. I was glad to hear that the authors of the paper did not carry this question to its logical conclusion, and advise artificial feeding. The flaw in the figures is probably due to incorrect information with regard to the feeding of the infants. As had already been pointed out by one of the previous speakers, very few of the native infants are entirely breast-fed. This is also true in Siam. As a rule, at the third month, but often earlier, in the latter country mothers are in the habit of supplementing their milk by feeding their children on softboiled rice, uncooked bananas, and frequently on other articles of diet of a far more indigestible nature.

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[2] *Tuba*, a fermented juice derived from the cut flower of the coconut palm. On standing for a day or two, it ferments and forms an intoxicating drink.

I have always been of the opinion that the high death rate among infants is the result of digestive troubles brought on by all the mixtures rammed down these poor infants' gullets, but that the condition produced might be beriberi is a new consideration to me. However, the subject of infant mortality is of supreme importance in any country. It is in Siam and no doubt in the Philippine Islands as well, so that I hope the mother will always be kept to the fore in the work of this association.

Dr. Victor G. Heiser, Director of Health for the Philippine Islands professor of hygiene, Philippine Medical School, Manila, P. I.—This paper is a most valuable contribution on the subject of infant mortality in the Philippines, and is, I believe, in spite of all that has been said and written upon this question, the first scientific work which has been done for the purpose of ascertaining the actual cause of death in a series of cases.

I feel that a statement should be made in regard to the statistics relating to naturally and artificially fed infants. Several years ago the Bureau of Health was requested to collect statistics showing whether the deaths which occurred among infants under one year of age were in cases which had been naturally or artificially fed; at that time I demurred because of the improbability of obtaining reliable figures of this nature by inquiries made by a clerk. It is well known to those who have experience in the Philippine Islands that almost from birth it is the custom to give rice, potatoes, and other solid food to children that are nursing. Anyone who has the least doubt in regard to the accuracy of this statement can easily satisfy himself by going through any native town and observing the children, and in a comparatively few observations he can witness mothers engaged in this practice. Furthermore, it is characteristic of the more ignorant classes to reply to questions of this nature in the manner in which they believe an answer is desired, so that when death certificates are presented and the family is asked whether the child had been artificially fed or breast-fed the mother would probably reply breast-fed, and perhaps deny other forms of feeding if she thought such an answer to be wanted.

One year ago, however, at the urgent request of a number of physicians of the city, I reluctantly gave instructions to have statistics of this kind gathered and as you perceive, according to them, 70 per cent of naturally fed children have died, which fact alone indicates that from our present knowledge of infant feeding these figures are not likely to be correct. I desire to disclaim all responsibility on behalf of the Bureau of Health for the statistics which have been used in the paper just read covering this particular point. However, in view of the showing just made, an investigation will be made on this point which will be based upon actual observation of infants in their homes.

The authors of this paper are to be congratulated upon the excellent manner in which they have presented this matter and the concise and clear arrangement of their statistics. They have made a valuable contribution concerning the cause of infant mortality in the Philippines, and with the data brought to light by Doctor Aron we should soon be in position to take effective steps to reduce the mortality.

Dr. Paul Clements, of the Bureau of Health, Manila, P. I.—I have been engaged to a certain extent on the other end of the work described by Doctors McLaughlin and Andrews. About 30 cases in which the pathologic diagnosis was infantile beriberi were sent to the morgue from my station, and it fell to my lot to collect the clinical histories. With one or two exceptions the patients all were babies under three months of age and the large majority were between one and two months. In the course of this work the clinical picture of the disease has assumed quite as much distinctness in my mind as Doctor Andrews says the pathologic picture has in his; and I have no doubt whatever that the disease is a distinct clinical and pathologic entity. My own investigations among the people with regard to the age at which mixed feeding of Filipino babies is commenced leads me to agree more fully with Doctor Highet than with any of the other gentlemen who have spoken on this subject. I have rarely, not often, seen babies younger than three months who were breast-fed and at the same time received only a negligible quantity of other food.

With regard to the name by which we still designate this pathologic entity, it seems that the authors of the paper have merely followed the nomenclature adopted by the first Japanese observer. The condition has been clearly recognized by some Filipino practitioners, and I believe Doctor Albert was the first to call the attention of the profession to its existence. The local name *"taon"* might perhaps be accepted.

Dr. Antonio G. Sison, second assistant resident in clinical medicine, Philippine Medical School, Manila, P. I.—The name malnutrition suggested by Doctor Aron as the cause of high infant mortality instead of beriberi, I think to be more reasonable because of the following: First, the high infant mortality is for the greater part among the poorer class. The women of the working class are at work most of the time and can not feed their babies properly and so are compelled to leave their children to the care of ignorant brothers or sisters, who give the infant anything they have at hand whenever it cries. Second, even if the babies are fed solely on the breast, the mother, because of her ignorance, usually gives her breast to her baby every time it cries, and this practice, in time, leads to malnutrition. Third, the poorer class of women who have been delivered in the hospitals of Manila, and there are taught to feed their infants properly, leave the hospital when they have recovered and never return for the treatment of the child if it becomes ill. For the reasons stated above, I believe the high infant mortality in the Philippines to be due to malnutrition, and this high mortality can be decreased by bettering the conditions of the poorer class socially and above all by educating them with respect to the care of their children.

Dr. Fernando Calderon. professor of obstetrics, Philippine Medical School, Manila, P. I.—It is doubtless true that babies purely breast-fed up to three months die of a disease called *"taon,"* possibly infantile beriberi. I have patients who have borne children all of whom were purely breast-fed, and nevertheless these children died at the age of three months. For this reason, I think that the establishment of institutions like the Gota de Leche[3] will be a great factor in decreasing the high infant mortality. Instead of having one such institution, we should establish ten to twenty in our city. Of course, the founding of charities of this class must be associated with the education of women of the poorer classes in the proper feeding of their children.

Dr. Vernon L. Andrews, Bureau of Science, assistant professor of pathology and bacteriology, Philippine Medical School, Manila, P. I.—In these cases we have a pathologic entity, and while we do not positively maintain it to be moist beriberi, yet we know of no better name for the condition, and if one can be suggested we will be glad to adopt it. We believe that this pathologic entity to be brought about by a nutritional disturbance. It is similar in many respects to moist beriberi in adults. Nearly all of these infants we have examined were under two and one-half months of age, and while this does not preclude the mothers from having given them a mixed diet, we feel that the giving of extraneous material is a negligible quantity in such early infancy. Furthermore, the majority of these infants were children of beriberic mothers, that is, of women in whom symptoms of beriberi were present.

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[3] An institution in Manila, established in 1904, devoted to providing pure milk at a small price to the poorer classes.

As to malaria being a causative factor in producing convulsions in these cases, I can only say that the blood was not examined, as the infants were not seen clinically. In one or two instances I found an enlarged spleen and a liver of a chocolate-brown color.

Dr. Allan J. McLaughlin, Assistant Director of Health, assistant professor of hygiene, Philippine Medical School, Manila, P. I.—I wish to correct a false impression which Doctor Musgrave has gathered from our paper. We have never dogmatically said that this disease is beriberi. By referring to our paper it will be noted that we belive we have demonstrated a pathologic entity responsible for many deaths of infants and for which we know of no better term than moist beriberi. Perhaps Doctor Musgrave can suggest a better one; if so, we shall be happy to substitute his diagnosis, tentatively at least, until the question of name is ultimately decided.

In regard to his statement that there are no breast-fed children, strictly speaking, in the Philippines, I desire to state that we are perfectly cognizant of the very common practice among the poorer classes of Filipino mothers of giving young children a variety of solid food in addition to the supply drawn from the breast; but this does not constitute artificial feeding, and the fact remains that the bulk of the children of the Filipino poor are mainly breast-fed. The majority of the deaths from the disease in question, which we tentatively term beriberi, occur in infants under three months of age.

The pernicious custom of giving solid food to the children is not usually practiced until after the infant is three or four months old. We admit, as Doctor Musgrave has suggested, that many Filipina mothers are tubercular, but this condition can only be considered as another factor in the poor nutrition of the Filipina mother. Tuberculosis is not hereditary and a diligent search for tubercular lesions in the cases under discussion produced negative results.

DISCUSSION ON THE PAPER, "UNSOLVED HEALTH PROBLEMS PECULIAR TO THE PHILIPPINES," BY DOCTOR HEISER.

Dr. H. Campbell Highet.—I have listened with great pleasure to Doctor Heiser's paper and at the same time with the deepest sympathy. Those of us who are engaged in administering sanitary measures in the Tropics all know the extent of the task set us and all of us have suffered from the want of funds. In fact we are often apt to think that our respective governments show but little sympathy with us, so small is the appropriation allowed for sanitary work, but, as Doctor

Heiser truly says, it is for us to do the best we can with our limited means and to discriminate carefully along what lines we should work.

Doctor Heiser has submitted an extended programme for the future, a programme which would really prove to be a Herculean task, but it is a good thing to see that he is hopeful of ultimate success. It is well, however, that those of us who have had the privilege of seeing something of the actual working of the Bureau of Health should look back and consider what had already been done to improve the sanitary condition of the people. In a matter of nine years the American Government has worked miracles, and I am certain that my fellow-delegates will join with me in heartily congratulating the Bureau of Health, and especially Doctor Heiser, on their great work.

Dr. J. M. Atkinson, principal medical officer, Hongkong, delegate from the Government of Hongkong.—I have much pleasure in seconding Doctor Highet's remarks congratulating Doctor Heiser on what has already been accomplished by the Bureau of Health. As far as I am aware, there is as yet no other example in the history of the world where such effectual measures have been taken to improve the sanitary condition of the subject native races those as which have been undertaken by the American Government since its occupation of these Islands, a period of less than twelve years.

To protect 6,000,000 people out of a total of 9,000,000 from smallpox is a wonderful piece of work. With regard to the city of Manila and its freedom from malarial fever, it appears to me that this freedom may be only temporary, as were the Filipinos to become infected with malaria, all the white people living in the city would be liable to infection. Mosquitoes capable of transmitting the malarial parasite are already present and extensive areas of swampy land exist.

I would suggest the advisability of gradually filling in these swamps as funds permit, as it is impossible effectually to drain them, since much of the area is below the level of the high tides prevailing. The filled-in swamps could be utilized for building sites, etc., and thus prove remunerative.

DISCUSSION ON THE PAPER, "THE PARTHENOGENESIS OF THE FEMALE CRESCENT BODY," BY DOCTOR NEEB.

Dr. E. R. Stitt, surgeon, United States Navy, associate professor of medical zoölogy, Philippine Medical School.—I have frequently, upon questioning others, found that they had never observed the phenomenon of parthenogenesis in connection with the benign tertian parasite, the species upon which Schaudinn made his observations.

In careful and repeated examinations of the blood of the large number of marines at the Naval Hospital in Washington, who had never been infected in Panama, and in which blood there were large numbers of gametes, no appearances which would indicate parthenogenetic division were noted. Within the past few months I have observed at Cañacao Naval Hospital a case in which there had been repeated attacks of malaria covering a period of one year. Upon examining the blood of this individual, numerous macrogametes were observed but no schizonts. A few days later parasites resembling Schaudinn's diagram of parthenogenesis were observed, and a few days later the man had a typical malarial paroxysm and in his blood numerous nonsexual macrogametes were visible, and as the microscopic appearance of the parasites showing sporulation, differed from that of the ordinary merocyte I was convinced that the phenomenon I observed was that of parthenogenesis of *Plasmodium vivax*.

Dr. H. M. Neeb.—I wish to add to my paper that fig. 5 is given in the work of Professor Ruge. The difference between fig. 5 of my paper and Ruge's is that Ruge gives a figure of a red blood cell in which are to be seen two parasites—one is a segmenting tertian parasite, the other next to it is a gamete. But in my plate a protoplasmic band combines both halves of this parasite. I can also absolutely state that this figure represents one parasite, and not a mixed infection of the red blood cell.

DISCUSSION ON THE PAPER, "MALARIAL FEVER DURING THE PUERPERIUM," BY DOCTOR ATKINSON.

Dr. Aldo Castellani, professor of tropical medicine and lecturer on dermatology, Ceylon Medical College, delegate from the Government of Ceylon.—I quite agree with Doctor Atkinson that in a malarial country quinine should be given to pregnant women. This is the rule I always follow in those districts of Ceylon where there is malaria, giving 5 grains (0.3 gram) every day and 10 grains (0.6 gram) once a week. Lately I have frequently used euquinine, which is said to have less action on the uterus than the ordinary preparation of quinine.

I also agree with Doctor Atkinson when he says that in malignant malaria larger doses of quinine must be given. It is probable that in a temperate zone 1 gram (15 grains) a day is sufficient to stop an infection with malignant malaria, but in tropical countries, like East Central Africa and Ceylon, I find that much larger doses must be given. In some cases 2 to 2.6 grams 30 or 40 and more grains a day are often necessary.

Doctor Atkinson.—I was not aware that euquinine had less effect on the uterine muscles than quinine. We always give euquinine to children ering from malaria because it has no taste and hence is easier to ainister.

I encountered a number of cases of malaria in the year 1889, after great rainfall which we had in Hongkong. You probably have all rd of this downpour during which 30 inches (900 millimeters) fell twenty-eight hours. As a natural result much malaria developed at t time, and at least 12 malignant cases came to the Government Civil spital.

Dr. J. M. Phalen, captain, Medical Corps, United States Army, mem- of United States Army Board for the Study of Tropical Diseases as y Occur in the Philippine Islands.—While recognizing the necessity large doses of quinine in exceptional cases, I wish to call attention a danger which is present in administering such large amounts. It t infrequently happens that impaired vision supervenes, dating from e time of the administration of quinine in doses which are not to be garded as excessive. I am not referring now to the quinine amaurosis ming on suddenly and causing more or less temporary blindness, but a gradual diminution of visual acuity apparently due to the action of inine on the optic nerve. I am strongly of the opinion that quinine ould be given in the minimum dosage that will control the disease.

Doctor Atkinson.—In reply to Doctor Phalen's statement concerning e occurrence of amaurosis after the giving of quinine, all I can say is at in my experience of practically hundreds of cases in which the ug has been given, I have never seen this result.

DISCUSSION ON THE PAPER, "SOME CLINICAL ASPECTS OF MYCETOMA, AN UNUSUAL FORM OF CALLOSITY COMPLICATING IT," BY MAJOR HOOTON.

Dr. J. M. Atkinson.—During my stay in Hongkong I have seen three ses of mycetoma, or Madura foot—one in a Chinaman, the other two Indians. The fact that we occasionally see these diseases in Hongkong due to the cosmopolitan nature of the population of that port.

I would like to ask Major Hooton what treatment he adopted in case umber 2, and if scraping will cure the disease?

In Hongkong the Chinese frequently suffer from a carinous affection alled "by-head." In this affection all the bones of the face and head ecome enormously enlarged. It has occurred to me that this may be lue either to mycetoma or actinomycosis.

Doctor Musgrave.—I enjoyed hearing Major Hooton's paper. The ubject of mycetoma is a very large one and I think that we will bring order out of chaos only by systematic study. The variations in culture of *Streptothrix* are greater than in any other organism. It must be remembered that none of these *Streptothrix* infections are inflammatory processes. They are destructive without much inflammation.

As to actinomycosis, I think perhaps it had better be included in the list of the *Streptothrix* infections.

Doctor Atkinson.—In connnection with *Streptothrix* infections, I should like to ask Doctor Musgrave and Major Hooton if there is any similar infection in horses in their respective countries? We have something approaching it in China.

Doctor Musgrave.—So far as I know there has been only one case reported in a native animal of the Philippines. I have seen it in Australian and American horses.

Maj. A. Hooton, I. M. S., Rajkot, Kathiawar, India, delegate from the government of India.—I will state in reply to Doctor Atkinson's question that the treatment I adopted in that particular case was the removal of the growth.

As regards the question of *Streptothrix* infection in animals, I made inquiries in Bombay and was told that perhaps two or three cases of mycetoma in animals are encountered in a year.

THIS NUMBER CONTAINS PAPERS READ AT THE FIRST BIENNIAL MEETING OF THE FAR EASTERN ASSOCIATION OF TROPICAL MEDICINE, HELD AT MANILA, MARCH 5 TO 12, 1910.

THE PHILIPPINE
JOURNAL OF SCIENCE
B. MEDICAL SCIENCES

VOL. V AUGUST, 1910 NO. 3

A STATISTICAL STUDY OF UNCINARIASIS AMONG WHITE MEN IN THE PHILIPPINES.[1]

By WESTON P. CHAMBERLAIN.[2]

The subject of hookworm disease at the present time is so much before the public that it may be of interest to consider in detail one feature of the situation, namely, the occurrence of the disease among adult American males in these Islands. Of all the infections which commonly are included in books on tropical medicine there are few, if any, which have such a wide distribution geographically, and especially such a range in latitude as uncinariasis. It is found in many regions that can lay no claim to being tropical, or even subtropical. Therefore, when studying the origin of the disease among Americans in the Philippines, it is necessary to consider two widely separated sources of infection: First, the Philippine Islands, and, second, certain parts of the United States where the disease is endemic.

OPPORTUNITIES FOR INFECTION IN THE PHILIPPINES.

When a white man in the Philippines is found to be harboring hookworms one is apt to assume that he became infected in the Islands, and a study of helminthiasis among the natives shows that opportunity for soil contamination is not lacking.

The first extensive work performed along this line was the examination of

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held in Manila, P. I., March 7, 1910.

[2] Major, Medical Corps, U. S. Army, president of the U. S. Army Board for the Study of Tropical Diseases as they occur in the Philippine Islands.

4,106 Filipino prisoners at Bilibid Prison (2) where 52 per cent were found to be the hosts of uncinaria, though rarely were these infections severe ones (3). The great majority of these prisoners were adult males. As high as 60 per cent of infections has been reported among Philippine Scouts in the United States Army (2). These high rates among Scouts and at Bilibid apparently are not a correct index of the prevalence of hookworm infection in the general population, if the results of subsequent work can be taken as representative. In the medical survey of Taytay (4), a representative Tagalog town in Luzon, 1,000 persons were examined and 11.6 per cent were found infected (males, 17.2 per cent; females, 6.6 per cent). The greatest number of worms recovered from any case was 14, and all worms found were of the species *Necator americanus*. Few of the infected ones presented any symptoms which could be attributed to hookworms, and the percentage of hæmoglobin in the infected cases was rather higher than in the noninfected.

Of 385 native women and children examined in Manila, 13 per cent were hosts of uncinaria. In the town of Las Piñas (5), Rizal Province, an examination of 6,000 people, completed by the Bureau of Health, September 30, 1909, showed 16.13 per cent infected with hookworms (males, 24 per cent; females, 8 per cent). A still more recent examination of 2,500 persons in the Cagayan valley showed 11.15 per cent of infection (males, 21 per cent; females, 9 per cent; children, 2 per cent).

The above figures from these widely separated localities in Luzon indicate that the infection for the general population of this island probably does not exceed 15 per cent, which is very low as compared with that in many other tropical countries; India showing from 65 to 83 per cent (2) and Porto Rico 90 per cent or more. This fact is surprising when one considers the habits of the natives, namely, careless disposal of excreta, bare feet, impure water supply. Furthermore, the agricultural pursuits of the inhabitants, combined with excessive moisture and rank vegetation, should, theoretically, lead to almost universal hookworm infection. The parasites seem to cause little disability among the Filipinos, and uncinariasis apparently is of slight economic importance here. This again contrasts sharply with conditions in Porto Rico. However, the disease is sufficiently common in the Philippines to lead to very general pollution of the soil and hence to the possible infection of white men.

OPPORTUNITIES FOR IMPORTATION FROM THE UNITED STATES.

The prevalence of uncinariasis among the inhabitants of the southern portion of the United States has been the subject of so much recent literature that I shall merely refer to the fact that the condition is extremely general throughout this region, many investigators, in large series of cases, having found 50 per cent of infections, and some claiming that 90 per cent of the rural population of certain sections is suffering from uncinariasis (11) (12) (14) (15) (16) (17).

The feature which especially pertains to my present subject is the prevalence of helminthiasis among United States soldiers, because the great majority of the white men whom I have been able to study in the Philippines either are or have been in the military service.

The first work on the occurrence of uncinariasis among American soldiers who had never been outside of the United States, was done by Siler (6) in 1909, when he found that out of 108 southern recruits 93, or 85 per cent, were infected. Following this investigation, I studied the subject among recruits received at Jackson Barracks, near New Orleans, with the result that of the southern-bred recruits arriving at that station, 67 per cent were shown to harbor *Uncinaria americana* (7). Further work proved that among 100 southern-bred[3] soldiers in their first enlistment period (three years) 60 per cent were infected, while among 33 men who had served more than one enlistment, only 11 per cent harbored the parasite. All of my cases were very mild infections and did not come from one section, every State in the South being represented. The details are shown in Table IV.

As this condition had hitherto been overlooked entirely, and consequently untreated, it follows that for ten years the Army had been bringing into the Philippines a continuous supply of men infected with the American hookworm. Perhaps we may facetiously call this one of our many ways of "Americanizing" the Islands. Just how many such men have come it is impossible to say, but there must have been several hundred annually. Southern-bred civilian employees of the Army and of the Insular Government have undoubtedly swelled these numbers.

This importation of uncinaria suggests the interesting question as to whether the United States was the origin of the American hookworm in the Philippines. All the early cases reported from here were diagnosed as the Old World species (notably Craig's 18 cases (8) referred to later). Recent reports as to both natives and whites, when they specify species at all, mention only the New World worm. However, it seems more reasonable to assume that the discrepancy is due to the limited knowledge of uncinaria which was possessed by most physicians ten or twelve years ago. Probably both species existed in the Islands, side by side, from the start, as is found to be the case in Panama (9).

The majority of the affected American soldiers return to the United States with their regiments in about two years. A few remain behind to fill civil positions and a few are transferred into other regiments just arriving in the Islands. It follows, therefore, that only a small minority of the Americans in the Philippines at any one time are likely to have infections which they brought from the homeland. In these, if reinfection is avoided, the worms gradually die out. My work with soldiers indicates that after a lapse of three years at least four-fifths of the hookworm carriers have freed themselves of their parasites. Somewhat similar results were obtained among infected soldiers in Cuba (20).

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[3] The term "southern-bred" in this article refers to those men who were born or had lived for a considerable time in some one or more of the following States: Maryland, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida, Alabama, Mississippi, Louisiana, Texas, Kentucky, Tennessee, Arkansas, and Missouri.

THE OCCURRENCE OF UNCINARIASIS AMONG AMERICANS IN THE PHILIPPINE ISLANDS.

Few of the soldiers recruited in the United States present any clinical evidence of uncinariasis and infections after arrival in the Philippine Islands should be comparatively rare, especially of late years, in view of the universal care exercised by the Army as to clothing, food, and water. Therefore, one would not expect to find hookworm disease widely prevalent among the Americans in the Islands. A study of the literature and statistics confirms this expectation.

While it is known that cases of agchylostomiasis were being detected during the early days of the American occupation (1898–1900), I can find no record of examinations, and the first available report is that of Strong in 1900 (22). Craig (8), in 1902, chronicled 18 cases found at the General Hospital in San Francisco among soldiers returning from the Philippine Islands. All of his cases seem to have been severe ones, and he states that the parasite in each instance was the Old World species.

In 1907 Cole (10) reported that since the organization of the Division Hospital at Manila, in 1898, the entire number of cases of uncinariasis among officers and men of the Regular Army in that institution had been 76. The total number of white admissions during this period is not stated and can not now be determined with accuracy, but it must have been over 25,000. This shows that uncinariasis was either very rare, or was rarely recognized. Of Cole's 76 cases, 38 were admitted for uncinariasis and 38 for other conditions, the ova of hookworm being found during the examination of the stools.

To determine what numbers of Americans of late years are showing infections with uncinaria, I have examined the records of the Division Hospital for the period from June 14, 1905, to January 29, 1910. A trifle over 8,200 white patients have been admitted and the ova of hookworms have been demostrated in the fæces of 71, a rate of infection of considerably less than 1 per cent. Deducting the number of duplicate examinations made in the positive hookworm cases, there have been over 8,000 examinations of stools during the period in which the 71 cases of uncinariasis have been found. This shows its great infrequency. The details of the positive cases are shown in Table I.

As the Division Hospital is used mainly for the more serious and chronic cases of disease, it occurred to me that a larger proportion of infections with uncinaria among the white soldiers might be shown in the records of the Army posts, since there the simpler cases of disease would receive treatment and be cured. Therefore, I examined the records of Fort William McKinley, a brigade post 6 miles from Manila. For the period from January 21, 1907, to January 25, 1910, there were found only 19 cases of uncinariasis, the admissions for the same period having numbered 11,514 persons, and the number of stool examinations (omitting repeated examinations) approximately 800. The percentage of patients found to be infected is, therefore, less than 0.2 per cent, this being about one-fifth of the rate at the Division Hospital. The percentage of stools showing ova of uncinaria was 0.9 per cent at the Division Hospital and 2.4 per cent at Fort William McKinley. (See Table II.)

The stools of 326 white patients were examined at the Civil Hospital in Manila, during the last half of 1909, and 16 cases of uncinariasis discovered, an infection rate of 4.8 per cent, which is very much higher than was found at the two hospitals referred to above. This hospital treats all classes of civilian employees who, on the average, probably take less care as regards shoes, food, and water than do the inmates of the military hospitals. The figures for the Civil Hospital were furnished by Doctor Ohno, of the Biological laboratory, Bureau of Science, Manila, P. I.

Of the 90 cases at the Division Hospital and at Fort William McKinley, only 11 (4 at the Division Hospital and 7 at Fort William McKinley) were admitted because of uncinariasis, the remainder of the cases having entered the hospital for other reasons, the ova being demonstrated upon the examination of the stools.[4] Therefore we are justified in considering that uncinariasis, sufficiently marked to be detected either clinically or by the routine stool examination, is rare among Americans in and about Manila.

Probably, if an exhaustive examination was made of the stools, with uncinariasis alone in view, a somewhat larger percentage of infection would be found than is shown above. By an exhaustive examination is meant the complete search, if necessary, of 8 or 10 cover-glass preparations from each patient, or the employment of the specific gravity method described by Bass (16) (17). My own experience in Louisiana showed that in 28 per cent of the infections 2 or more cover-glass preparations had to be gone over to demonstrate the ova and sometimes 6 or 8 were examined before the first egg was discovered. As far as is known, the only work of this kind, on a large scale, which has been done in the Islands, was the examination of the Eighth Infantry at Camp Jossman, Guimaras, by Lieutenants Pinkston and McIntire, under the direction of Major Glennan (19). They examined 528 men and found 9 per cent infected with hookworms.

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[4] Of the 76 cases of uncinariasis among officers and soldiers found by Cole at the Division Hospital from its organization in 1898 up to August, 1907, one-half (38) were admitted for uncinariasis, and the histories of these 38 show gastro-intestinal disturbance in 32, of whom 21 had dysentery, 5 diarrhœa, and 1 sprue. Of the 38 men admitted for other conditions, in whose stools ova of uncinaria were found, all had gastro-intestinal symptoms (10).

CAUSES OF ADMISSION AND ASSOCIATED DISEASES.

A study of Tables I and II, pages 251–262, and 263, shows that the cause for admission in the 90 men harboring hookworms was uncinariasis in 11 cases, and for the remaining 79 as follows:

TABLE III.

Cause of admission.	Number of cases.	Cause of admission.	Number of cases.
Dysentery	24	Dengue	7
Diarrhœa	7	Malaria	4
Enteritis	6	Surgical	2
Sprue	6	Cardiac, organic	2
Gastritis	2	Tuberculosis	5
		Venereal	2
		Miscellaneous	9
		Unknown	3
Total gastro-intestinal	45	Total other than gastro-intestinal	34

It is notable that among 90 men found to have uncinariasis, gastro-intestinal troubles were the cause of 50 per cent of the admissions, the coexistence of dysentery and uncinariasis being especially common. This coincidence is possibly explained in part by the fact that the stools of diarrhœa and dysentery patients were thoroughly examined for the possible presence of amœbæ and the hookworm ova discovered accidently, while the fæces of the patients having no enteric symptoms were not always examined and consequently mild cases of uncinariasis, without clinical signs, may frequently have escaped notice.

However, there are two other possibilities: First, that the presence of uncinaria lowered the vitality, thereby favoring the development of gastroenteric diseases, and, second, that the infection with hookworms occurred by mouth at the same time that the causes of dysentery gained entry. Study of the case histories throws no light on these points.

SYMPTOMATOLOGY.

It is unnecessary to describe the classical symptoms of hookworm disease as given in the textbooks. A review of the histories of the 71 cases at the Division Hospital proves that such a train of symptoms is rare in the class of patients this paper deals with. Anæmia was not at all a prominent symptom. In a few instances in which the hæmoglobin was estimated it was indeed low, ranging from 40 to 85 per cent, but in all these patients there were ample causes for anæmia other than the hookworm. Cole found that in his series anæmia, dyspnœa and œdema were not marked (10). Wolf was struck with the fact that the majority of patients in the Philippine Islands harboring uncinaria appeared to be in excellent health (6). Table III shows how commonly gastro-intestinal symptoms were associated with uncinariasis, and also that usually the presence of an intestinal parasite was unsuspected until the stool examination showed ova. This is in accord with my experience at New Orleans, where uncinariasis was found extensively among men apparently in perfect health.

The few differential leucocyte counts which have been recorded at the Division Hospital in uncinariasis confirm my observations at New Orleans that an eosinophilia of over 5 per cent is the rule, but that figures as low as 1, 2, or 3 per cent are by no means infrequent and are valueless in excluding the diagnosis of hookworm disease (7).

WHERE THE AMERICANS IN THE PHILIPPINE ISLANDS CONTRACT THEIR INFECTIONS WITH UNCINARIA.

About a year ago, in reporting my work in the United States, I expressed the opinion that when soldiers with uncinariasis (species not mentioned) returned from the Philippine Islands it was unsafe to assume that the infection had occurred in the Islands, as there was quite as much likelihood that these men had taken the worms from the United States and had returned with them still in the intestine. With the view of establishing or disproving this theory, I have investigated the residences of the 90 cases covered by this report. As the histories did not record the various places of residence of each patient, I obtained from the sick and wounded report cards and from the descriptive lists of the soldiers, whenever possible, the following data which I shall term "residential factors."

1. Place of enlistment or acceptance for enlistment.
2. Birthplace, giving State of the United States, or country, if not in United States.
3. Residence of the man's nearest relative.
4. Residence of the man himself as given at the date of enlistment.

In the cases of the soldiers at Fort William McKinley and most of the civilians, only the birthplace could be determined.

An analysis of these data shows that among the 90 cases of uncinariasis 44 were born in the southern portion of the United States, 41 elsewhere, and in 5 there is no record. In the case of each of the 44 men born in the Southern States for whom other "residential factors" could be obtained, it was found that at least one, and usually two, other factors designated the South. Therefore, it seems fair to assume that these 44 southern-born men, constituting 49 per cent of the cases of uncinariasis, were so definitely identified with the South that the infection of the majority of them with hookworm, while in that region, was highly probable.

In connection with southern birth and residence it is necessary to consider also length of service in the Army, because, under the good sanitary conditions prevailing in the military service within the limits of the United States, I assume that reinfection with hookworms must be extremely rare, and that, under such sanitary conditions, after five years' service the greater part of the soldiers who were infected at the date of their enlistment will have become free from the parasites by reason of the natural death of the worms. Looking over Tables

I and II with this point in mind, it is seen that 14 of the southern-born men (cases Nos. 7, 15, 19, 21, 23, 26, 29, 33, 34, 39, 41, 74, 77, 87) had served in the Army five years or over at the date of current admission on sick report, and therefore had probably freed themselves of any original infection and had gained their present infection in the Philippines during this or a previous tour of duty.

Deducting these 14 long-service men from the 44 southern-born men, leaves 30 cases out of the 90 (33 per cent) in which it appears probable that the hookworm infection may have originated in the United States and have been imported into the Philippines. Of course it is impossible to prove that these men may not have received additional infections while in the Islands.[5]

There is, with one or two exceptions, nothing in the histories and residences of the 41 cases not born in the South, to indicate that the infection occurred elsewhere than in the Philippine Islands. Just how the worms gained entry into the intestines in these cases is an interesting subject for speculation.

It is rare for a civilian or a soldier in the peaceful times of the last few years to run much risk of contracting ground itch, since good shoes are universally worn, and the persons considered are not engaged in agricultural pursuits, or severe field service. Great efforts are made to provide safe drinking water and well-prepared food for all Americans, but that sufficient care in this respect is not always taken seems evident from the numerous cases of dysentery that continue to occur. In view of these facts, it seems probable to the writer that infection with hookworms among Americans in the Philippines occurs more commonly by mouth than through the integument.

IMPORTANCE OF TREATING MILD UNCINARIASIS.

Although this investigation shows that hookworm infections among Americans in the Philippines are rarely found and that such as are encountered present little clinical evidence of the disease, I do not think that the importance of the condition should be underestimated. From observations on soldiers in New Orleans I concluded that while the light infections did not materially affect the efficiency of the man doing garrison duty at home, nevertheless, he was somewhat more energetic and felt better after the expulsion of the worms. It is probable that even a few parasites, by injuring the intestinal mucosa, by disturbing digestion, by secreting toxins, by producing a slight anæmia and by altering the normal proportions of the different varieties of leucocytes, usually at the expense of the polynuclears, must to some extent lower the vitality, thereby predisposing to various infections, especially in active military service. Even a slight lowering of vitality is of importance in the Tropics where the white man is confronted by so many serious diseases awaiting an opportunity to overcome his natural resistance. Therefore, in view of the ease of microscopic diagnosis and the success of vermifuge treatment, it seems desirable that all white residents of the Tropics should be examined at intervals to determine if they serve as the hosts for uncinaria. The importance of this is emphasized by the frequency with which uncinaria were found associated with gastro-intestinal diseases, especially sprue, diarrhœa, and dysentery, which are the arch enemies of the white man in the Tropics.

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[5] Since writing this article I have received some additional statistics from Camp Jossman. Out of 66 cases of uncinariasis (found between December 18, 1907, and March 19, 1908) in the Eighth Infantry, 16 were from southern States, a percentage of 24. Deducting 12 men with over five years' service, leaves only 4 cases, or 6 per cent of the total, in which it appears likely that the men brought their present infections from the United States, unless they were reinfected at their homes while on furlough. Out of 20 cases of uncinariasis in the Fourth Infantry, which relieved the Eighth at Camp Jossman (period from April 11, 1908, to December 14, 1909), 16 were from southern States, a percentage of 75. Deducting 5 long-service men, leaves 11 cases, or 55 per cent, in which there is a likelihood that their present infection originated in the United States. As the Fourth Infantry had newly arrived in the Islands (April 1, 1908), the high proportion of southern-born men found infected correctly indicates the influence of southern birth on uncinaria infection. The Eighth Infantry had been in the Islands about a year and a half when the first examinations were made and it shows no predominance of infection among southern-born men, which goes to indicate that a large proportion of these men were infected in the Islands during their two years of service.

I am indebted for these statistics to First Lieut. Alexander D. Parce, Medical Corps, United States Army.

CONCLUSIONS.

1. Uncinariasis is found among the Filipinos in probably not over 15 per cent of the general population and is mild in type and of small economic importance.

2. The percentage of infections is higher in adult males, reaching 50 or 60 per cent among the Filipino Scouts and Bilibid prisoners.

3. The average percentage of infection of the white population of the southern part of the United States is probably much higher than the rate among the Filipinos.

4. From 65 to 85 per cent of the southern-bred white recruits for the United States Army are infected with uncinaria, usually mildly, and these infected soldiers have been coming in considerable numbers to the Philippines, thus importing *Uncinaria americana.*

5. The majority of these soldiers, if not reinfected, become free from the worms by natural processes in about five years.

6. Uncinariasis, sufficiently marked to be evident clinically, is very rare among American men in the Philippine Islands.

7. Even a routine stool examination among Americans shows few cases, 71 out of 8,000 examinations at the Division Hospital and 19 out of 800 examinations at the Fort William McKinley Hospital.

8. An exhaustive stool examination among Americans in the Philippine Islands would probably show a somewhat greater frequency.

9. Of the 90 cases of uncinariasis found at the above hospitals, only 11 were admitted for uncinariasis. Forty-five were admitted for gastro-

intestinal troubles, dysentery, diarrhea, and sprue being the most frequent causes.

10. In 30 out of 90 cases (33 per cent) there is a probability that the infection originated in the United States and was imported into the Philippine Islands.

11. In the remaining 60 cases it is probable that infection occurred in the Philippine Islands, and there is reason to believe the parasites were usually introduced through the mouth with food or water.

12. Uncinariasis is of sufficient importance among Americans in the Islands to make an occasional careful search for ova desirable.

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TABLE I.—*Cases of uncinariasis at the Division Hospital, Manila, P. I., from June 14, 1905, to January 29, 1910 (during this period approximately 8,200 white patients were admitted).*

(A) SOLDIERS.

Case No.	Age.	Years of service.	Place enlisted.	Birthplace.	Residence of nearest relative.	Residence.	Occupation before present enlistment.	Cause of admission to hospital.	Years of P. I. service.	Remarks.
1	22	1	Montana	Alabama	Alabama	Alabama	Carpenter	Dengue	½	
2	31	4	Massachusetts	Massachusetts	Massachusetts	Massachusetts	Laborer	Tuberculosis	4	Died in California.
3	31	4	California	Indiana	Indiana	Army	do	Dengue	2	
4	23	2	Ohio	West Virginia	West Virginia	West Virginia	Miner	do	½	
5	21	2	do	do	Virginia	do	do	do	½	
6	47	23	Texas	Ohio	Ohio	Army	Soldier	Tuberculosis	1	
7	28	8		Virginia				Fever		
8	22	1	New York	New York	New York	New York	Driver	Enteritis	1	
9	21	2	North Carolina	North Carolina	North Carolina	North Carolina	Farmer	Malaria	1	
10	24	3	Ohio	Georgia	Georgia	Georgia	Tinner	Fever	2½	
11	25	1	West Virginia	West Virginia	West Virginia	West Virginia	Farmer	Diarrhœa	1	
12	22	½	Illinois	Montana	Montana	Montana	Clerk	Dysentery	½	
13	38	11	District of Columbia	Holland	New Jersey	Army	Soldier	Diarrhœa	1½	
14	25	8	California	Pennsylvania	Montana	do	do	Dysentery	½	
15	28	5	Alabama	South Carolina	South Carolina		Bridge builder	do	1½	
16	26	1	Kansas	Illinois	Illinois	Illinois	Laborer	do	1	
17	31	4	New York	Ireland	New York	Army	Soldier	do	½	
18	25	2	Massachusetts	Massachusetts	Virginia	Massachusetts	Fireman	do	2	
19	32	7	Philadelphia	Montana	Montana		Soldier	do	3	
20	23	4	Kentucky	Kentucky	Kentucky	Kentucky	Farmer	Diarrhœa	1	
21	35	14		Mississippi				Sprue	6	
22	23	2	West Virginia	Kentucky	Kentucky	Kentucky	Farmer	Tuberculosis	1½	
23	26	6½	New York	North Carolina	England	Tennessee	Soldier	Bubo	3	Uncinaria americana.
24	35	8	Georgia	Ireland	New York	New York	do	Dysentery	3	

TABLE I.—*Cases of uncinariasis at the Division Hospital, Manila, P. I., from June 14, 1905, to January 29, 1910, etc.*—Continued.

(A) SOLDIERS—Continued.

Case No.	Age.	Years of service.	Place enlisted.	Birthplace.	Residence of nearest relative.	Residence.	Occupation before present enlistment.	Cause of admission to hospital.	Years of P. I. service.	Remarks.
25	33	2½	Wisconsin	Wisconsin	Wisconsin	Wisconsin	Bookkeeper	Dysentery	1½	
26	26	6½		Mississippi	Mississippi	Army	Soldier	Gastritis	1½	Uncinaria americana.
27	42	18	New York	Sweden	New York	do	do	Dysentery	1½	Do.
28	33	8	Washington	Wisconsin	Wisconsin	Wisconsin	do	Fever	2½	
29	50	10	West Virginia	West Virginia	West Virginia	West Virginia	do	Uncinariasis	1½	Uncinaria americana; probably other P. I. service.
30	37	15	New York	Ireland	Illinois	Illinois	do	do	1½	Uncinaria americana.
31	23	1	Tennessee	Tennessee	Tennessee	Tennessee	Laborer	Diarrhœa	1	
32	35	12		Ireland	Ireland		Soldier	Enteritis	5	7 months in Porto Rico.
33	33	11	Kansas	Kansas	Kansas	Army	do	Syphilis	1½	
34	32	9		Alabama				Gastritis		
35	34	6	Texas	North Carolina	North Carolina	North Carolina	Soldier	Hepatitis	½	Ankylostoma [illegible]
36	19	1	Louisiana	Louisiana	Louisiana	Louisiana	Student	Diarrhœa	1	
37	34	10	Colorado	Ireland	Pennsylvania	Colorado	Soldier	Enteritis	2	
38	25	4½	Texas	Kentucky	Kentucky	Army	do	Diarrhœa	1	
39	26	5	do	Georgia	Georgia	do	do	Dengue	1	
40	40	16		Scotland	England			Syphilis		
41	24	1	Alabama	New Jersey	New Jersey	Alabama	Engineer	Uncinariasis	1	[illegible]
42	18	½	Kentucky	Kentucky	Kentucky	Kentucky	Teamster	Fever	½	
43	22	2	do	do	do	do	Farmer	Malaria	1	
44	31	10	Utah	do	Maryland	Army	Soldier	Dysentery	1½	
45	30	7		Illinois	Illinois	do	do	Sprue	½	
46	24	2	Illinois	do	do	Illinois	Barber	Jaundice	1	

47	32	11	Philippine Islands	New York	New York	Army	Soldier	Cardiac	3	Organic lesion.
48	26	3	California	Georgia	Georgia	Georgia	Railroad	Tuberculosis	6	Died in Philippine Islands.
49	40	17	do	New York	Louisiana	Army	Soldier	Dysentery	7	
50	25	2	Illinois	Indiana	Indiana	Illinois	Clerk	Enteritis	2	
51	28	6		Illinois	Illinois	Army	Soldier	Cardiac	3½	Organic lesion.
52	25	4	Virginia	New Hampshire	New Hampshire	do	do	Enteritis	1	
53	23	2	Texas	Texas	Texas	Texas	Telegrapher	do	1½	
54	20	2	Kentucky	Kentucky	Kentucky	Kentucky	Motorman	Dengue	1	
55	22	2	Florida	Georgia	Georgia	Georgia	Painter	Dysentery	1½	
56	34	8	Minnesota	Norway	Minnesota	Army	Soldier	Fever	2½	
57	31	2	Pennsylvania	Tennessee	Tennessee	Tennessee	Clerk	Dysentery	1½	
58	23	2	Kentucky	Kentucky	Kentucky	Kentucky	Farmer	Sprue	2½	

TABLE I.—*Cases of uncinariasis at the Division Hospital, Manila, P. I., from June 14, 1905, to January 29, 1910, etc.*—Continued.

(B) CIVILIANS.

Case No.	Age.	Birthplace.	Residence of nearest relative.	Occupation in the Islands.	Cause of admission to hospital.	Years of P. I. service.	Remarks.
59	30	New York	New York	Quartermaster employee	Malaria	9	
60	32	Kansas			Tuberculosis		
61	32	Ohio	Pennsylvania		Uncinariasis		
62	43	New Jersey	Montana	Teamster	Sprue	5	Ankylostoma duod.
63					Dysentery		
64					do		
65	26	Florida	Florida	Carpenter	do	5	
66	40	Washington	Washington		Migraine		
67	29	Denmark			Dysentery		
68	27	Massachusetts	Massachusetts		Sprue		
69	39	Illinois	Canada		Dermatitis		
70	47	Virginia			Dysentery		
71	29	Ohio			Hemorrhoids		

Total, 71 cases.

Seventy-one cases of uncinariasis among 8,200 patients is a proportion of 0.87 per cent.

The number of stool examinations during this period was over 8,000, and of these examinations 0.9 per cent showed ova of uncinaria.

No mention is made of the species of worm except in the cases noted in "remarks."

In the case of reënlisted men the occupation is usually given as "soldier" without regard to the occupation he may have had before his first enlistment.

TABLE II.—*Cases of uncinariasis recorded at Fort McKinley, P. I., from January 21, 1907, to January 26, 1910 (during this period 11,544 patients were admitted).*

Case No.	Age.	Years of service.	Birthplace.	Cause of admission to hospital	Remarks.
72	23	2	Kentucky	Agchylostomiasis	
73	23	2	do	Malaria	
74	30	11	North Carolina	Dysentery	
75	23	3	Kentucky	do	
76	28	1½	Ohio	do	
77	35	7	Georgia	Agchylostomiasis	
78	23	2	Italy	do	
79	23	1	Tennessee	Dysentery	
80	22	½	do	Uncinariasis	
81					No records.
82	24	3	New York	Dysentery	
83	22	1	West Virginia	Dengue	
84					Do.
85	26	1	Texas	Agchylostomiasis	
86					Do.
87	31	12	Alabama	Diarrhœa	
88	22	7	Hungary	Uncinariasis	
89	24	1½	Russia	do	
90	37	16	Ireland	Sprue	

Total, 19 cases.

Nineteen cases of uncinariasis among 11,544 patients is a proportion of less than 0.2 per cent.

The number of stool examinations made during this period was 800, and of these examinations 2.4 per cent showed ova of uncinaria.

TABLE IV.—*Showing the character of the cases of uncinariasis being imported into the Philippine Islands. Details are given of 60 cases of uncinariasis found among 100 unselected southern-bred white soldiers, who were in their first enlistment and had never been outside of the United States.*[a]

Case No.	Age.	Height.	Weight.	Occupation at time of enlistment.	Occupation previous to enlistment.	Birthplace.	Residence before enlistment.	History of ground itch.[b]	Years since ground itch.	Color.	Hæmoglobin.	Polynuclears.	Eosinophiles.	Lymphocytes, small.	Lymphocytes, large.	Transitionals.	Mast cells.	Number of ova found in stools.[c]	Number of worms found after treatment.
		In.	*Lbs.*								*P. ct.*	*P. ct.*	*P. ct.*	*P. ct.*	*P. ct.*	*P. ct.*	*P. ct.*		
1	22	66	124	Farmer	Farmer	Mississippi	Mississippi	N.		Good	100	62.0	6.5	22.0	7.0	2.5	0	Many	18
2	21	68	133	do	do	do	do	P.	12	do	100	66.5	8.5	16.5	5.5	2	1	do	42
3	23	69	135	Plumber	None	South Carolina	Alabama	P.	14	Pale	80	74.5	2	15	3.5	5	0	Few	0
4	18	66	127	Factory	Farmer	Mississippi	North Carolina	P.	14	Good	100	44	26	22	4	4	0	do	3
5	24	68	145	Farmer	do	do	Mississippi	P.	14	Pale	80	46	7	26	11.5	9.5	0	do	17
7	19	66	118	Laborer	Laborer	do	do	?		Good	90	40	20.5	25.5	4	5	0	Very few	?
8	23	68	128	Collector	Farmer	Georgia	Louisiana	P.	15	do	90	60.5	7.5	20	7	4.5	0.5	?	33
9	20	66	126	Lumber	do	Texas	Mississippi	P.	9	do	90	63	11	17	6	3	0	Many	10
10	28	68	153	Engineer	do	Alabama	do	P.	20	do	80	47	8.5	32	7	5.5	0	Very few	2
11	22	69	144	Farmer	do	do	Alabama	P.	12	Fair	80	69	7	15.5	4	3.5	1	Very many	12
12	27	66	130	Carpenter	do	Mississippi	Mississippi	P.	18	Pale	90	62.5	15	9.5	3.5	9	0.5	Few	5
14	23	72	151	Barber	do	Florida	Louisiana	P.	7	Fair	80	51.5	17	23	2.5	5	1	Very many	?
15	18	67	150	Laborer	do	West Virginia	do	N.		Pale	90	49	11	28.5	5.5	5	1	Very few	0
16	26	67	129	do	do	Alabama	Alabama	P.	20	Good	90	68	5	23	2.5	1.5	0	Few	1
17	29	69	152	Factory	do	do	do	P.	5	Pale	90	71.5	4.5	18	3	2	1	do	?
18	23	72	150	Farmer	do	Georgia	Georgia	P.	15	Good	80	65	10.5	14	3.5	6.5	0.5	Very many	0
20	23	72	147	Stable	do	Alabama	Alabama	P.	12	Pale	100	68	4	20	6	2	0	do	2
22	21	64	126	Machinist	do	Louisiana	Louisiana	P.	12	Good	100	58.5	5.5	29	4.5	2.5	0	Very few	16
23	22	70	152	do	do	North Carolina	Panama	N.		Excellent	100	60	7	25	5	2	1	Many	1

25	27	71	150	Laborer	do	Texas	Texas	N.		Good	90	31	5	50	7.5	6.5	0	do	24
26	21	69	157	Farmer	Logging	Mississippi	Mississippi	P.	8	do	100	68.5	8.5	16.5	3.5	2.5	0.5	Few	1
28	21	71	154	Mill man	Farmer	North Carolina	do	P.	10	do	90	50	23	15	8	4	0	do	2
31	19	70	149	Laborer	do	Mississippi	do	N.		do	90	73	6	13	5	3	0	Very many	5
32	23	70	157	Farmer	do	Louisiana	Louisiana	N.		do	90	54	26	13	3	2	2	Very few	7
33	23	69	138	do	do	North Carolina	North Carolina	P.	14	do	100	46	10	28	9	5	2	Few	19
34	18	69	125	do	do	Alabama	Alabama	N.		Fair	90	40	10.5	35.5	8	5.5	0.5	Very many	11
35	21	68	129	Laborer	do	Louisiana	Louisiana	N.		Good	90	35.5	7	32.5	11.5	18.5	0	do	75
41	27	67	148	Farmer	do	Maryland	Maryland	N.		do	90	70	6	14	4	6	0	Very few	1
42	22	67	138	Showman	do	Kentucky	Alabama	N.		Pale	100	65	2	22	5	6	0	do	1
45	23	68	143	Fireman	Fireman	Mississippi	Mississippi	N.		Good	90	56	4	31	7	2	0	Many	2
47	21	67	126	Farmer	R. R. laborer	do	do	P.	7	Pale	80	63	7.5	21	2.5	3	0	Very many	82
48	23	69	166	Fireman	Farmer	do	do	P.	10	do	100	64	6	23	4	3	0	Many	35
50	29	70	146	Engineer	do	Alabama	do	P.	?	Good	90	53.5	7.5	29.5	4	5.5	0	Very few	2
51	19	65	145	Farmer	do	do	do	P.	?	do	90	42.5	8	37	7.5	4	1	Many	35
52	22	66	115	do	do	do	do	N.		do	90	16	12	32.5	6.5	2.5	0.5	Very many	13
53	26	69	140	Laborer	do	do	do	P.	12	do	100	58	4	36	1	1	0	Very few	3
54	20	68	144	Smith	Smith	Mississippi	do	N.		do	100	62.5	4.5	26.5	2.5	3.5	0.5	Few	4
57	19	65	143	Canning	Canning	Texas	Louisiana	N.		do	90	60	7	24	4	5	0	do	0
58	23	70	138	Fireman	Farmer	Louisiana	Mississippi	P.	2	do	90	66.5	2.5	25.5	2.5	3	0	do	55
60	25	70	135	Sawmill	do	Mississippi	do	P.	18	do	90	30	6	32	15	17	0	do	13
62	31	65	115	Lumbering	do	do	do	P.	18	do	100	63	8	21	3	2	0	Many	31
63	23	69	136	Pile driving	do	Florida	Louisiana	N.		do	90	65	5	24.5	1.5	4	0	Few	11
65	29	65	138	Machinist	do	do	Florida	P.	4	Pale	90	41	5	48	2	1	0	do	32
66	22	69	132	Express	Express	Texas	Texas	N.		Fair	90	54	6	32.5	3	3	1.5	Very few	1
68	23	66	146	Clerk	Farmer	Alabama	Alabama	N.		Good	90	55	5	26	5	7	0	Few	18
69	23	69	130	Farmer	do	Louisiana	Louisiana	N.		do	90	59	13	23	2	2	1	do	10
70	22	70	151	Logging	do	Mississippi	Mississippi	P.	3	do	90	49	11.5	28	6	5	0.5	do	1
72	26	70	164	Laborer	Farmer	Georgia	Georgia	N.		do	100	62	5	23	5.5	1.5	0	Very few	13
73	21	68	151	Coal miner	Lived on farm	Alabama	Alabama	N.		do	100	52	8	37	3	0	0	Many	27

[a] The average hæmoglobin in the 60 infected men was 91 per cent, and in a series of 70 noninfected southern soldiers it was 94 per cent. The average eosinophile count in 60 infected cases was 8.5 per cent, and in a series of 83 noninfected it was 2.2 per cent.

[b] N. means negative history for ground itch; P. means positive history for ground itch.

[c] If 1 or 2 ova were found per cover-glass, the record was "few." If at least 2 cover-glasses were gone over before the first egg was found the record was "very few."

TABLE IV.—*Showing the character of the cases of uncinariasis being imported into the Philippine Islands, etc.*—Continued.

Case No.	Age.	Height.	Weight.	Occupation at time of enlistment.	Occupation previous to enlistment.	Birthplace.	Residence before enlistment.	History of ground itch.	Years since ground itch.	Color.	Hæmoglobin.	Pulynuclears.	Eosinophiles.	Limphocytes, small.	Lymphocytes, large.	Transitionals.	Mast cells.	Number of ova found in stools.	Number of worms found after treatment.
		In.	*Lbs.*								*P. ct.*	*P. ct.*	*P. ct.*	*P. ct.*	*P. ct.*	*P. ct.*	*P. ct.*		
75	19	67	132	Laborer	Laborer	Mississippi	Mississippi	P.	5	Pale	100	83	6	9	1	1	0	Very many	77
78	21	70	160	Cotton mill	Farmer	Alabama	Florida	P.	7	Fair	100	62	4	26	6	2	0	Few	75
79	22	69	137	Fireman	Scholar	Mississippi	Mississippi	P.	12	Good	100	53	4.5	33	4.5	5	0	Very many	99
81	25	68	159	Lumbering	Farmer	Alabama	Alabama	P.	15	do	100	54	1	27.5	10	7.5	0	Very few	1
82	23	68	165	do	do	do	do	P.	11	do	90	48	11	31	4.5	3.5	2	do	3
83	23	68	132	Electrician	Electrician	do	do	N.		Fair	90	24.5	13.5	51	5	5	1	Very many	38
86	23	64	123	Laborer	Laborer	Mississippi	Mississippi	N.		do	80	45.5	3.5	35	10.5	5.5	0	Very few	5
87	28	74	175	Farmer	Farmer	do	do	P.	10	Good	100	35.5	7	42.5	9	5	1	do	15
93	24	68	137	Mill man	do	do	do	P.	10	do	160	38	12	47	1	1	1	Very many	24
96	23	65	138	Brakeman	Mill hand	North Carolina	South Caralina	P.	15	do	100	62.5	3	24.5	4	6	0	Few	10
97	22	66	140	Circus man	Farmer	Texas	Louisiana	N.		Pale	80	56	12.5	28	1.5	1	1	do	0

THE PREVALENCE OF INTESTINAL PARASITES IN RIZAL AND CAVITE PROVINCES AND IN CAGAYAN VALLEY.[1]

By R. S. Kissler[2] and Liborio Gomez.[3]

Shortly after the completion of the medical survey of the town of Taytay,[4] the Bureau of Health organized a campaign for the purpose of examining and treating the natives of certain provinces infected with intestinal parasites, with the especial view of determining the prevalence of hookworm infection and its relation to the public health.

The first headquarters of this field party was located at Las Piñas, in the Province of Rizal. The town has a sandy soil and is situated by the seaside. When the work was completed there, the field party was sent to the Cagayan Valley, having its headquarters at Tuguegarao, Cagayan Province, an inland town about 100 kilometers from the mouth of the Cagayan River. Later it was located at Santa Isabel, a hacienda of the Compañía Tabacalera, in the municipality of Ilagan, Isabela, about 60 kilometers further inland from the mouth of the river.

It was found necessary to treat all patients affected with disease in order to induce large numbers of the people to come to the dispensary. Hence, many who were examined for intestinal parasites were found to be suffering from other diseases. The results obtained are based upon the examination of one single cover-glass preparation, but in a few doubtful cases two or three such preparations were examined. Most of the stools studied were passed on the day the examination was performed, but a few were passed the day before. In the beginning of the work an attempt was made to administer magnesium sulphate, but as a rule the patients, after accepting their medicine, never came back, and later the plan of previously administering purgatives was given up entirely.

Babies under 1 year of age were not included in the examinations, as at the beginning of the work it was noted that the stools of those examined were negative, their food being chiefly mother's milk.

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[1] Read at the biennial meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 12, 1910.

[2] Medical Inspector, Bureau of Health, Manila, P. I.

[3] Assistant, Biological laboratory, Bureau of Science, Manila, P. I.

[4] *This Journal, Sec. B* (1909), 4, 207.

The present report covers the period from June, 1909, to February 8, 1910, during which time the party was in the field. Further work is being pursued in the districts near at hand and this will be reported upon when the studies are completed.

About three-fourths of the cases examined at Las Piñas resided in other towns of Cavite and Rizal Provinces. The principal occupations of the people are fishing and working in the rice paddies and salt beds. The same may be said of the majority of inhabitants coming from other towns of these provinces, although in the latter the percentage of the people that do not actually work on the farm or at the fisheries or salt beds is greater, many of them being of the wealthier classes, such as landowners and merchants, while others are employed at the navy yard and railroad.

Many of the people examined in Tuguegarao, such as landowners, merchants, employees, and school children, did not actually work on the farm. The great majority of the inhabitants of the Cagayan Valley are much more ignorant than those of the provinces situated nearer to Manila and hence they hesitate more in submitting to medical treatment than do the enlightened classes. It should be emphasized that the majority of the enlightened Filipinos, and consequently those having greater confidence in scientific medical treatment, do not, as a rule, work on the farm.

The actual working class in the hacienda of Santa Isabel was examined, and in this investigation the field party was greatly assisted by the manager and the municipal officer.

The people here are almost entirely occupied in planting and cultivating tobacco, and for this purpose much field work is necessary. The men plow the land and with the women do the planting. When the tobacco stalks are sufficiently large, men, women, and the older children examine every plant in order to rid it of any worms present. Consequently, during the whole season of growth the workers are almost constantly in the fields. The soil consists of loose clay.

INFECTIONS WITH ASCARIS.

Contrary to the findings of Garrison[5] at Bilibid Prison, we found *Ascaris lumbricoides* to be the most prevalent intestinal parasite. In Las Piñas, 77.21 per cent of the whole population is infected; in Tuguegarao, 73.51 per cent, and in Santa Isabel, 60.59 per cent. The infection is greatest among children and greater in adult females than in adult males, as is shown by the examinations made at Santa Isabel, namely, 70.58 per cent in children, 53.31 per cent in females, and 51.09 per cent in males.

INFECTIONS WITH TRICHURIS.

Garrison[6] found this infection to be the most frequent in his 4,106 cases in Bilibid Prison. However, we found it to be second to *Ascaris*. This difference may be due to the fact that Garrison's statistics in Bilibid Prison are based for the greater part on an adult male population. In

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[5] *This Journal, Sec. B* (1908), 3, 191.

[6] *Ibid.*, 197.

Las Piñas, 53.40 per cent of all the cases examined were infected, and 25.90 per cent in Tuguegarao. However, the number of cases infected with *Trichuris* in Santa Isabel fell much below the average, being only 6.23 per cent.

INFECTIONS WITH HOOKWORMS.

Hookworm infection was found to be third in frequency in the examination for intestinal parasites. In Las Piñas 11.14 per cent of all the cases examined were infected; in Tuguegarao, 8.01 per cent. In Santa Isabel we found the highest percentage of infection in all our work, 45.38 per cent.

The adult males show the highest rate; 20.91 per cent in Las Piñas, 13.52 in Tuguegarao, and 60.58 per cent in Santa Isabel. Adult females are less infected; 9.45 per cent in Las Piñas, 8.05 per cent in Tuguegarao, and 51.26 per cent in Santa Isabel. Children are infected to a much lesser degree: 2.63 per cent in Las Piñas, 3.66 per cent in Tuguegarao, and 26.42 per cent in Santa Isabel.

The strikingly high percentage of infection in Santa Isabel may be due to the occupation of the people, which requires almost constant exposure of their bare feet to the soil in the fields while caring for the tobacco plants. Again, the population is concentrated in a single spot on the hacienda. The soil, being clayey, is not particularly favorable to this infection.

We noticed fissures on the plantar surface of the feet in many individuals found harboring the hookworm, but these did not appear to cause any discomfort except an occasional itching sensation. Upon examination we were not able to demonstrate any embryonic form of the hookworm in these lesions. However, on account of the discovery of these fissures on the feet and the greater prevalence of the hookworm in adult males, although we have found no evidence of *Uncinarial dermatitis*,[7] we are inclined to think the skin transmission is an important means of infection with this parasite.

Clinical symptoms.—Cases exhibiting typical symptoms of uncinariasis are rare. A few persons have complained of discomfort in the abdominal region which has been relieved entirely by treatment which resulted in the expulsion of the hookworms. Several cases in the Santa Isabel hacienda were picked out by the manager as being typically lazy, but upon examination they were not found to harbor this parasite. One of these cases showed emaciation together with great pallor of the conjunctivæ, without any history of malaria or tuberculosis. The examination of the blood in general demonstrated an increase of the eosinophile leucocytes. The absence of clinical symptoms was probably due to the paucity of the infecting worms. In most cases only five or ten were expelled after treatment, in others only two or three.

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[7] Stelwagon, Henry W. Philadelphia and London, 5th ed. (1907), 1109.

INFECTIONS WITH STRONGYLOIDES.

The distribution of this parasite varies according to the locality. Garrison[8] in 1908 found 3 per cent infected among the Bilibid prisoners. In 1901 Strong[9] reported 13 cases of *Stronglyloides* (0.6 per cent) among 2,179 persons examined in the Philippines. We found 135 persons infected (2.24 per cent) in Las Piñas, but not a single case in Tuguegarao and Santa Isabel.

INFECTIONS WITH OXYURIS.

The statistics regarding this parasite can not be accurate, for we depend for its diagnosis upon the finding of the egg which is laid outside the anus and which often does not appear with the fæces. We found 4.95 per cent in Las Piñas, 2.62 per cent in Tuguegarao, and 1.24 per cent in Santa Isabel.

INFECTIONS WITH AMŒBÆ.

Previous examinations of stools made in the Philippines have shown a high percentage of *Amœbæ*, varying from 20 to 70 per cent. Gilman[10] reported 32 cases showing active amœbic ulcerations out of 100 autopsies at the Philippine Medical School. Musgrave and Clegg[11] found 26 per cent and Garrison[12] 23 per cent of the immates of Bilibid Prison infected. Garrison, Leynes and Llamas[13] found 2.7 per cent in Taytay.

Our figures are still lower, we having found but 0.39 per cent infected in Las Piñas. Nearly all of these were free from clinical symptoms. In Tuguegarao and Santa Isabel we did not find a single case of infection and a typical stool with blood and mucus was not seen.

INFECTIONS WITH FLAGELLATES AND CILIATES.

In Las Piñas we found 3.88 per cent infected with monads and 0.14 per cent with *Balantidium coli.* In Tuguegarao 3.73 per cent with monads and in Santa Isabel 1.49 per cent. Neither the *Balantidium coli* nor any other ciliate was found in these two places.

INFECTIONS WITH TAPEWORMS.

Taenia saginata was most frequently found. Only 4, or 0.06 per cent, out of 6,000 cases examined at Las Piñas were infected with tapeworm. In Tuguegarao the percentage is eight times higher, 0.50 per cent, and in Santa Isabel twenty times, 1.37 per cent. The high percentage in these places may possibly be due to the importation of European cattle by the Compañía Tabacalera. We did not find a single case of infection with *Tænia solium* among the natives. Only one instance of the infection was encountered in a Spaniard in Cabagan, Cagayan, and this has not been recorded.

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[8] *This Journal, Sec. B* (1908), 3, 201.

[9] Report of the Surgeon-General, United States Army (1901), 203.

[10] *This Journal, Sec. B* (1908), 3, 217.

[11] *Ibid.* (1906), 1, 909.

[12] *Ibid.* (1908), 3, 200.

[13] *Ibid.* (1909), 4, 257.

HYMENOLEPIS.

The previous reports on *Hymenolepis* have been meager. Garrison[14] found five infections in his Bilibid cases. The Taytay field party does not record a single case.[15] However, in Tuguegarao we found 0.26 per cent infected in adults and 0.46 per cent in children; in Santa Isabel, 1.73 per cent in children and 0.36 per cent in adult males. The majority of the cases had no clinical manifestations of disease, a few showed diarrhœa with mucus.

FLUKES.

Thus far in our work in these provinces we have found no flukes, either in the blood or sputum examined.

SUMMARY.

The result of our work is in accord with that of other authors regarding the almost universal infection of the whole population of the Philippine Islands with intestinal parasites.

The chief infections in the districts covered by this report are from *Ascaris* and *Trichuris*, and their distribution is rather uniform, although in Santa Isabel the percentage of infection with *Trichuris* fell very low.

The distribution of the hookworm varies, Santa Isabel showing the highest percentage ever recorded in the Islands. Males were more affected than females. The percentage of hookworm infection does not appear to be affected by the nature of the soil on which the people live.

The distribution of *Amœba* shows still greater variation. In and around Manila the percentage of infection is higher, but in the Cagayan Valley it is rather low.

Infection with *Hymenolepis*, while not found in Cavite and Rizal Provinces, is rather frequent in the Cagayan Valley. Children are mainly infected.

Tapeworms are also more frequent in Cagayan and Isabela than in Cavite and Rizal.

The parasite known as the worm of Cochin-China diarrhœa, or *Strongyloides intestinalis*, was not found in Cagayan and Isabela, whereas it was quite frequently encountered in Cavite and Rizal.

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[14] *Ibid.* (1908), 3, 205.

[15] *Ibid.* (1909), 4, 257.

Monads were found rather uniformly distributed in the cases, but ciliates were not encountered in the Cagayan Valley.

The results of these investigations are given in Tables I, II and III.

TABLE I.—*Santa Isabel.—January 20 to February 8, 1910.*

Examinations and infections.	Males.		Females.		Children.		Total.	
	No.	Percent.	No.	Percent.	No.	Percent.	No.	Percent.
Cases examined	274		238		288		802	
Positive	231	84.46	201	84.45	258	89.56	692	86.28
Negative	43	15.54	37	15.55	30	10.44	110	13.72
Cases infected with—								
Hookworm	166	60.58	122	51.26	76	26.42	364	45.38
Ascaris	140	51.09	127	53.31	219	70.68	486	60.59
Trichuris	14	5.10	26	10.92	10	3.43	50	6.23
Oxyuris	3	1.09	2	0.88	5	1.73	10	1.24
Monads	6	2.18	2	0.88	4	1.38	12	1.49
Hymenolepis	1	0.36	0	0	5	1.73	6	0.74
Tænia	8	2.92	3	1.26	0	0	11	1.37

TABLE II.—*Tuguegarao.—November and December, 1909.*

Municipalities.	Number of cases.	Males.	Females.	Children.	Ascaris.	Trichuris.	Hookworm.				Monads.	Oxyuris.	Hymenolepis.		Tænia.	Positives.	Negatives.
							Males.	Females.	Children.	Total.			Adults.	Children.			
Tuguegarao	2,218	896	474	1,048	1,694	578	100	39	38	177	89	60	3	11	9	1,615	603
Enrile	103	65	17	21	63	18	4	4	0	8	4	2	2	0	0	92	11
Solana	91	53	15	23	45	26	8	0	0	8	2	4	2	1	3	68	23
Cabagan Viejo and Nuevo	88	38	25	25	61	24	4	0	4	8	0	0	0	0	0	73	15
Peñablanca	21	8	4	9	2	8	0	1	0	1	1	1	0	0	0	15	6
Iguig	19	6	0	13	9	3	2	0	0	2	0	0	0	0	0	15	4
Alcalá	6	6	0	0	4	3	1	0	0	1	0	0	0	0	0	6	0
Abulug	4	0	0	4	4	0	0	0	0	0	0	0	0	0	0	4	0
Amulung	2	2	0	0	1	1	1	0	0	1	0	0	0	0	0	2	0
Tuao	2	0	2	0	1	0	0	0	0	0	0	0	0	0	1	2	0
Calamaniugan	2	0	2	0	2	2	0	0	0	0	0	0	0	0	0	2	0
Other towns	38	28	7	3	21	9	2	0	0	2	1	1	0	0	0	29	9
Total examinations	2,594	902	546	1,146	1,907	672	122	44	42	208	97	68	7	12	13	1,923	671
Total percentage	100	34.31	21.04	44.17	73.55	25.90	13.52	8.05	3.66	8.01	3.73	2.62	0.26	0.46	0.50	74.13	25.87

TABLE III.—*Report of the hookworm field party at Las Piñas, Rizal, as to the prevalence of intestinal-parasite-infection during the months of June, July, August and September, 1909.*

Municipalities.	Examination.	Males.	Females.	Children.	Hookworm.				Ascaris.	Trichuris.	Strongyloides.	Monads.	Ameba.	Oxyurius vermicularis.	Balantidium coli.	Trenia.	Blood.	Pus.	Mucus.	Positives.	Negatives.	Total hookworm.
					Total.	Males.	Females.	Children.														
																						Per cent.
Las Piñas	1,720	587	734	399	187	115	63	9	1,285	1,124	59	82	10	122	4	2	19	15	18	1,569	151	10.87
Bacoor	1,227	385	567	275	145	89	47	9	969	584	21	47	5	59	2	------	4	2	7	1,095	132	11.81
Imus	1,147	261	406	480	130	66	47	17	874	402	11	35	1	20	2	------	9	1	20	998	154	11.33
Parañaque	649	231	265	153	70	47	27	2	589	488	33	39	6	64	1	------	6	6	6	622	27	10.78
Cavite Viejo	356	114	148	94	35	20	13	2	279	171	4	9	------	14	------	------	1	------	2	320	36	9.83
Pasay	269	96	117	56	30	19	11	------	202	135	3	6	1	6	------	------	1	1	1	238	31	11.15
Binacayan	127	34	61	32	10	2	6	2	95	75	3	3	------	5	------	------	2	1	1	118	9	7.87
San Francisco Malabon	106	37	50	19	17	11	6	------	74	47	------	2	------	1	------	------	1	------	2	94	12	16.03
Dasmariñas	84	20	40	24	15	7	7	1	52	24	------	4	------	------	------	------	------	------	------	70	14	17.84
Cavite	66	21	29	16	4	3	1	------	46	38	------	------	------	5	------	2	1	------	------	59	7	6.06
Manila	49	9	36	4	5	2	3	------	30	28	------	1	------	------	------	------	------	------	2	40	9	10.20
Tansa or Santa Cruz Malabon	52	14	22	16	6	3	3	------	36	28	------	------	------	1	------	------	------	------	------	42	10	11.53
Salinas	45	21	18	6	3	2	1	------	37	23	------	1	------	1	------	------	------	------	1	42	3	66.66
Noveleta	37	16	10	11	6	3	3	------	27	16	------	2	1	------	------	------	------	------	------	32	5	16.21
Naic	16	5	9	2	------	------	------	------	11	7	------	------	------	------	------	------	------	------	------	14	2	.00
Silang	6	5	1	------	1	1	------	------	4	2	------	------	------	------	------	------	1	1	------	6	------	16.66
Caridad	8	2	3	3	1	1	------	------	5	2	------	1	------	------	------	------	------	------	------	5	3	12.50
Pasig	3	3	------	------	1	1	------	------	2	------	------	------	------	------	------	------	------	------	------	3	------	33.33
Malibay	3	1	2	------	------	------	------	------	2	2	------	------	------	------	------	------	------	------	------	3	------	.00
Taguig	3	1	2	------	------	------	------	------	2	1	------	------	------	------	------	------	------	------	------	2	1	.00
San Juan	2	1	1	------	2	1	1	------	------	2	------	------	------	------	------	------	------	------	------	2	------	100.00

San Roque	2	2							2	1										2		.00
Cainta	3		3						1	1										1	2	.00
Caloocan	2	1	1						2											2		.00
Malolos	2	2			1	1			2	1										2		50.00
San Rafael	2		1	1					2	2										2		.00
San Pedro Macati	2	2							2	1										2		.00
Batangas Province	6	2	4						3	3	1									5	1	.00
Laguna Province	2	1	1						2	2										2		.00
Miscellaneous	22	10	10	2	2		2		10	4		2								19	3	9.00
Total examinations	6,018	1,884	2,541	1,593	671	394	241	42	4,647	3,241	135	234	24	298	9	4	45	27	60	5,406	612	
Total percentage	100	31.30	42.22	26.48	11.14	20.91	9.48	2.63	77.21	53.40	2.24	3.88	0.39	4.95	0.14	0.06	0.74	0.44	0.99	89.83	10.16	11.14

MYZOMYIA ROSSII AS A MALARIA-CARRIER.[1]

By W. T. DE VOGEL.[2]

It has several times been pointed out that malaria frequently occurs in the Dutch East Indies near the seacoast; yet the fact remains that an anopheline species which develops in brackish and salt water, and even in concentrated sea water, and which has been found along the coast, can not be accepted as a satisfactory explanation of this phenomenon without further proof, for this particular anopheline is *Myzomyia rossii* Theob., and many writers allege that it does not seem to be capable of transmitting malaria.[3]

Giles[4] says that according to Daniels, of Calcutta, *Myzomyia rossii* can not be infected either with tertian gametes or with crescents. Theobald states the same thing.[5]

Dönitz[6] writes that Ross experimented in vain with this species and that the researches of Stephens and Christopher show that it has nothing to do with malaria.

In a report of the Wellcome Research Laboratories[7] the statement is made that "not every anopheline can carry malaria, as witness *Myzomyia rossii* in India."

Also Galli Vallerio and Rochaz de Jong[8] mention that this species does not appear to be able to transmit malaria. Here in Java it is very difficult to secure literature on the subject. Professor De Meyers, of Amsterdam, kindly informed me by letter that the 1907 edition of Theobald's "A Monograph of the Culicidæ of the World" contains the following on page 3: "*M. Rossii* is said not to be an active distributer in India, while Mr. Green says he is almost sure it is accountable for some of the outbreaks in Ceylon;" and on page 47, "the malarial parasite will develop in it, but it has not yet been found infected naturally. Mr. Green considers it to be the malarial carrier in parts of Ceylon, especially in the Batticoloa district. He found the larvæ breeding in the brackish lake at Batticolao town, and on the coconut estates he found them breeding in small water holes used for watering the young coconuts, and on some estates in earthenware chatties sunk at the base of the palms."

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 10, 1910.

[2] Chief medical officer, Samarang, Java.

[3] Cf. Banks, *This Journal, Sec. B* (1907), 2, 513; (1909), 4, 238. (ED.)

[4] A Handbook of the Gnats or Mosquitoes. London, 2d ed. (1902), 311.

[5] A Monograph of the Culicidæ of the World. London, 2d ed. (1901), 85.

[6] *Ztschr. f. Hyg. u. Infections-krankh.* (1902), 41, 15.

[7] *Second Rep. Wellcome Res. Lab., Khartoum* (1906), 27.

[8] Manual pour la lutte contre les Moustiques. (1906).

Manson[9] includes *Myzomyia rossii* in a list of anophelines "which have been shown with more or less precision to be efficient hosts of the malarial parasites." It is noteworthy that in the same edition Theobald, and also Giles and Dönitz, mention the names of Daniels, Ross, Christopher, and Stephens as having in vain attempted to show the capability of infection of *Myzomyia rossii;* and neither Theobald nor Manson gives the names of those who have been able to do so. Theobald only refers to the opinion of Mr. E. Green,[10] government entomologist at Ceylon, as to the part played by *Myzomyia rossii* in the epidemics of malaria which break out from time to time in the Batticoloa district of Ceylon. This seems to imply that he infers the infectibility from epidemiological data, and not from successful experiments. From this article it appears that Mr. Green has not made any experiments in transmitting the infection.

I have never found an infected specimen among the large numbers of individuals of *Myzomyia rossii* which I have caught and examined in my own house at Samarang.

Other Anophelinæ have been met with further inland, but never near the shore. Mosquito larvæ floating horizontally on the surface of the water have been collected in various degrees of contamination, and the mosquitoes developed from these larvæ resembled each other in all particulars.

In my publication "Anophelines dans l'eau de mer,"[11] I called this species "*Anopheles vagus*" from the description given by Dönitz.[12] Specimens obtained from larvæ bred in sea water and partially evaporated sea water were examined by Professor De Meyere, of Amsterdam, and he declared them all to be *Myzomyia rossii.* Indeed, Blanchard, among other authorities, also considers *Anopheles vagus* not to be a new species discovered by Dönitz, but as identical with *Myzomyia rossii.*

The absence of any other species which might presumably be a transmitter of malaria led to the question whether the reason why infection experiments with *Myzomyia rossii* had yielded negative results might not be found in the fact that up to the present time they had always been made with specimens bred in fresh water. Until quite recently it was not known that *Myzomyia rossii* is able to develop in water containing a high percentage of salt; the *M. rossii* caught in my house, which, as above stated, I had examined with negative results, were also derived from fresh water. This species, so frequently encountered near the seacoast, generally breeds in water containing a comparatively high percentage of sodium chloride. In connection with the prevalence of malaria near the coast, this fact leads to the supposition that possibly this high percentage of salt in the breeding places may offer a favorable condition for the transference of the gametes to the stomach of the mosquito and the further development of the parasites, i. e., it may render the mosquito more liable to malarial infection.

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[9] Tropical Diseases. New York, 4th ed. (1907), 147.

[10] *Trop. Agr.* (1909), 32, 84. Kindly sent me for reference by Dr. W. T. Hunger, of Salatiga.

[11] *Atti Soc. mal.* (1907), 8, 1–27.

[12] *Ztschr. f. Hyg. u. Infectionskrankh.* (1902), 41, 80.

Considered in this connection, the statement of Schoo, namely, that in the polders of North Holland malaria formerly raged more violently in those places where the water was brackish, acquires a special significance. At Samarang, it appears from the morbidity tables collected by Doctor Terburgh that the number of children with an enlarged spleen varies between 60 and 100 per cent in the native villages (*kampongs*) situated along the coast and the two overflow canals which carry brackish water far inland and which contain innumerable pools along their banks. Among the rice fields and fresh-water marshes farther in the interior, the numbers vary between 5 and 25 per cent. In the quarters of the town of Samarang situated farther from the coast, I have thus far found only two anopheline species, chiefly *Myzomyia rossii*, and much more rarely *Myzorrhynchus barbirostris* v. d. Wulp. (specimens determined by Theobald).

The larvæ which I have encountered in the rice fields near Samarang before and after the growing of the crops, as well as in fresh-water ponds and marshes, invariably developed into imagines, which, as far as I could observe, in every detail resembled specimens of *Myzomyia rossii* found along the coast. I have never found *Myzorrhynchus barbirostris* in the larval state, but always as an imago, and then very rarely. Although other anopheline species may occur at Samarang, it is certain that *Myzomyia rossii* far exceeds them in number, and forms the most important subject for malarial epidemiology here. Green[13] mentions that *Mysomyia rossii* also is the species occurring in the Batticoloa district. It is a remarkable fact in connection with the malaria epidemics which he mentions, that, in this district also, the breeding places were found along a lake containing brackish water. No other anopheline species found in our Archipelago is known to adapt itself so readily to the saline condition of the water in which the ova are deposited, as *Myzomyia rossii*.[14]

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[13] *Loc. cit.*

[14] I find it stated in the *Rev. of Some of the Recent Advances in Trop. Med.*, supplement of the *Third Rep. Wellcome Research Lab.* at the *Gordon Memorial College, Khartoum*, page 134, that in 1908 F. H. Foly and A. Yvernault published a paper entitled "Anophelines dans d'eau salée" in the *Bull. Soc. Path. Exot.* (1908), 1, 172, in which they say that in Algiers breeding places of the anopheline species *Pyretophorus chaudoyei* Theob. were found containing a high percentage of salt; and in the *Atti Soc. mal.* (1906), 7, that in Algiers, larvæ of *Anopheles maculipennis*, which occurs exclusively along the shore of the Mediterranean, were found in water containing 0.481 per cent of sodium chloride. It is also stated by Schoo that Nuttal, Celli, Ficalbi, Grassi, Centanni, Christopher and Stephens found larvæ in water containing 0.656 per cent sodium chloride, Perrone in 1.87 per cent, and Vivanti in 1.74 per cent sodium chloride.

No other species is known to be capable of developing both in fresh water and in partially evaporated sea water containing more than 5 per cent sodium chloride. This species, *M. rossii*, therefore, is especially suitable for determining the limits within which the quantity of salt contained in the breeding places may or may nor render the mosquitoes produced in them more or less liable to infection with malarial plasmodia.

Suitable subjects for making infection experiments on mosquitoes are rarely encountered among the sufferers from malaria in the Samarang hospitals. Gametes are generally found only sporadically in the peripheral blood. Consequently, on October 25, 1908, when a female patient, whose blood-smears under the microscope showed two or three Laveran crescents in every field, applied for admission to one of the hospitals, the opportunity was eagerly seized.

The patient was a young native (Javanese) woman from the Karang Bidara quarter situated within the district of malarial centers along the coast. She was extremely anæmic, and had a spleen that reached to the umbilicus. The pulse was regular. The temperature varied between 36° and 36.8°. Apprehending the ever-threatening pernicious attack, it was decided to give a dose of 0.500 gram of hydrochloride of quinine three times a day. This dose was administered daily from October 26 onward.

Meanwhile, mosquito larvæ were obtained along the coast from pools containing water of varying concentration, from rain water, up to solutions containing 1.6 per cent sodium chloride. After a few difficulties had been overcome, the first mosquito was dissected with a positive result. This was on November 3, and after the patient had taken 1.5 gram of quinine for nine days. The insect had sucked the patient's blood five hours previously.

The stomach, full of blood, was crushed under a cover-glass. When examined under the microscope, worm-like, moving organisms which resembled oökinetes were visible. The preparation was then stained according to Giemsa's method. Many spool-shaped elements were then seen, with an intensively colored chromatin core in the middle and the pigment compressed to one point in the spool. The picture exactly resembled the illustrations of oökinetes in colored preparations given by Schaudinn. Unfortunately, it is not known what percentage of common salt was contained in the water from which this mosquito was produced. The following table gives the results of these experiments, together with a few of the more important details:

No.	Date of feeding on patient's blood.	Patient took 1.5 grams of quinine hydrochloride per day—	Period elapsed after sucking the blood.		Percentage of NaCl in water from which mosquito was obtained.	Result of the experiments.
		Days.	*Days.*	*hrs.*		
1	November 3	9	0	5	(a)	Oökinetes; stained with Giemsa.
2	November 5	11	4	0	1.3	Numerous young oöcysts on stomach prep. in glycerine.
3	November 6	12	8	0	1.3	Many well-developed oöcysts and some almost ripe: preparation stained with alumcarmine inclosed in Canada balsam.
	November 9	15	5	0		
4	November 7	13	6	0	0.65	One oöcyst in stomach wall: preparation lost in further treatment.
5	November 7	13	8	0	0.6	One doubtful oöcyst in stomach wall.
	November 10	16	5	0	0.6	
6	November 8	14	11	0	0.6	No infection.
7	November 13	19	5	0	0.6	Do.
8	do	19	5	0	(b)	Do.
9	do	19	9	0	(b)	Do.
10	do	19	9	0	(b)	Do.

[a] Unknown. [b] Fresh, probably rain water.

Only a small number of mosquitoes were examined. Many larvæ did not develop, while the females which hatched were with difficulty kept alive for any length of time, and not a single one until the stage was reached in which sporozoites appear in the salivary gland. It is also true that some specimens were used for determining the species. A small number of the females could not be induced to suck the blood, and many of the specimens that did so died every day, so that very little resulted from our plan to examine different specimens at regular intervals in order to observe the whole course of development. It is extremely difficult to isolate the stomach even within a few hours after death. As I feared that the mosquitoes would not remain alive until the day fixed for their examination, the few remaining specimens were dissected in advance of that time. All this is to be regretted; for, whereas certainty might have been obtained, as it is, the results allow only of conjecture as to what effect the percentage of salt in the breeding places has upon the liability to malarial infection of the mosquitoes. It is true that the two mosquitoes taken from water containing 1.3 per cent sodium chloride were found to be strongly infected. In a few specimens taken from water with 0.6 per cent sodium chloride, the infection was either mild, dubious, or entirely absent, while not a single one of those obtained from fresh water proved to be infected. However, as it happened, those from water containing 0.6 per cent sodium chloride and also from fresh water, sucked the blood later than those from water with 1.3 per cent.

A gradual decrease was observed in the number of gametes in the peripheral blood during the time the patient was in the hospital, and this was strikingly apparent during the last days of her stay. During the first days, gametes were found in every field, and in the fresh blood the microgametes were seen repeatedly, swarming out of the microgametocytes. When the patient left on November 13, only a few crescents were discovered in the preparation after considerable search. On examining the fresh blood in the last days, many phagocytes were seen actively employed in absorbing the crescents, a clear proof of the way in which the human organism rids itself of this infection.

The diminished chances of infection when a much smaller number of gametes are present than there were originally, is an important factor, which must certainly not be neglected in considering the negative results of the last days of the experiment, when, as it happened, mosquitoes from water with a low or hardly any percentage of salt were tested.

Although, of course this inquiry in no way lays claim to completeness, yet where the chances of carrying out the experiments are so rare it seemed to me not out of place to publish the result, as at least it has been shown experimentally that *Myzomyia rossii* can be infected with *Plasmodium immaculatum*. This fact alone seems to me of no little importance, as, among other things, it clearly shows the way in which malaria may spread along the coast in our Indian islands. In order to be certain that the mosquitoes which I used in these experiments really were *M. rossii*, I sent the specimens of the same breed which we had kept for determination, to Professor Nuttall, of Cambridge, with the request that they might also be submitted to Theobald. I take this opportunity of expressing my sincere thanks to Professor Nuttall for the way in which, with his usual obliging kindness, he complied with my request.

All the specimens obtained from larvæ collected on six different dates from six different breeding places proved to be *Myzomyia rossii*. What remained of the mosquitoes 2, 3 and 5, after dissection, namely, the wings, legs, head with thorax and abdomen, was also sent in three separate tubes filled with alcohol and marked 2, 4 and 5. I was informed that Theobald said he was unable to effect a determination from the fragments sent to him. The chance that just these specimens should happen to belong to another species is too slight to be considered.

Although these experiments, made with the purpose of infecting *Myzomyia rossii* taken from water containing 1.3 per cent sodium chloride, may not in themselves lead to any definite conclusion, as to the positive influence of the salt contained in the breeding places upon the liability to malarial infection of *Myzomyia rossii* developed in such a solution, nevertheless the hypothesis that such an influence exists is supported by the probability that earlier experiments were unsuccessful because they were made with insects taken from fresh water. It may be presumed with some certainty that the liability to malarial infection is variable in the same anopheline species. We are quite in the dark when we attempt to point out the causes influencing this liability. Without any known reason we sometimes succeed, time after time, in our infection experiments, and then again, under apparently similar conditions, we are entirely unsuccessful.

There are districts where formerly malaria was extremely prevalent but where now the disease is rarely encountered (as in Tuscany), notwithstanding the fact that there is no decrease in the number of anophelines, and malarial subjects are imported into these regions from other parts, a fact which would lead one to expect an increase of malaria. Where no immunity has set in among the inhabitants, the causes of this phenomenon must be sought in a state of immunity in the prevailing anopheline species, arising from outward circumstances which did not exist before. A knowledge of the causes of such immunity might be a powerful weapon in combating malaria in epidemic form.

The results obtained from these few experiments seem to me to point a way which offers a chance of determining one of these causes with certainty. Finally, they confirm what has been shown by the experiments of Gualdi and Martirano and of Schaudinn, namely, that the gametes from blood containing quinine develop to oöcysts in the stomach of the anopheles mosquito.

ANTIMALARIAL PROPHYLACTIC MEASURES AND THEIR RESULTS AT THE NAVAL STATION, OLONGAPO, P. I.[1]

By A. W. DUNBAR.[2]

While the naval station proper at Olongapo has an enviable sanitary reputation, there has always been a large number of cases of malarial infection attributed to other places on Subig Bay, especially to the Marine target range at Maquinaya, distant about 4 miles. The exact reason why malaria should be comparatively rare at the station itself is not evident, as the presence of the anopheles mosquito and a large native contingent furnish the factors necessary to infect the force of approximately 1,000 men. The elevation of the quarters to a height of about 5 feet and the absence of vegetation probably have much to do with it.

In January, 1909, the hospital ship *Relief* was ordered to Olongapo to care for the large number of sick which overtaxed the small sick quarters. Incidentally, the utility of a hospital ship, even in the time of peace, was shown in this instance, as it furnished a mobile hospital which could be used to supplement those on shore in cases of unusual concentration of force, or in the event of an epidemic or serious catastrophe.

I will not burden this paper with the figures showing the amount of malaria then present at the station, but it suffices to say that about one man in ten was practically unfit for active service in the field. The seriousness of this can better be appreciated when it is understood that the two regiments of the Marine Corps at this station constitute the personnel of the advanced base and expeditionary force in case of hostilities in this part of the world.

By reviewing the medical records of the station and constructing a chart showing the admission for each month, the greatest increase of malaria was graphically shown to follow the opening of the target season at Maquinaya, other duties, such as practice marches, and the presence of a company at Mecmany Point erecting a battery, causing slight rises; while during the rainy season, when the Marines were more or less restricted to the barracks or station, there were but very few cases, and these were probably unreported infections continuing from past months. On the chart accompanying this paper, the admissions have not been reduced to percentages as the strength of the command was found to have been so nearly constant as to make its calculation unnecessary.

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 10, 1910.

[2] Surgeon, United States Navy.

At this time, abandonment of the range upon which there had already been considerable expenditure of money and labor, was seriously considered.

The Maquinaya range is located on a narrow sand spit between the sea beach and an impassable morass, into which flows a stream of considerable size which overflows much of the range during the rainy season. While considerable clearing of the range had already been done, there were both high grass and mangrove trees close to the camp, and anopheles mosquitoes were present in considerable numbers, especially in the evening when the breeze failed. The men were quartered in tents and slept on the regulation folding camp cot under nets. The protection from mosquito bites afforded by these narrow nets is more in theory than in practice, for a slight movement of the body or limbs during sleep results in contact with the net, permitting the mosquito to feed to its satisfaction without fear of molestation.

A board appointed for the purpose recommended (1) filling in of the swampy land on the range and further clearing of the ground so that there should be no shelter for the mosquito within at least 200 yards of the range; (2) the erection of thoroughly screened quarters for officers and men. These recommendations were carried out and the quarters completed by the date of the opening of the target season. The buildings are of light construction, elevated about 4 feet from the ground, well ventilated and completely screened.

RESULTS.

During the first quarter of last year there were 105 admissions to the hospital ship, giving 2,214 sick days, and the station sick quarters were constantly kept filled, and this has been the yearly experience since the range was established. During the elapsed part, over one-half, of the first quarter of this year, there had been 8 admissions to the hospital ship for malaria, giving 120 sick days, and there have been only 53 cases treated at the sick quarters.

Before concluding, a few words may be added regarding treatment. To you, accustomed to a tropical medical practice, this is not pertinent, but to the newcomer, acquainted with the mild infections of the Temperate Zone, yielding readily to quinine in 1 to 2 gram doses, the administration of 4 to 8 grams daily seems heroic, but thus has been found necessary here. The treatment is, as a rule, continued for three weeks, but not necessarily or usually in the larger doses. The worst cases we have had, being in a state of collapse requiring saline intravenously, were those who had repeated returns under the smaller doses.

ILLUSTRATION.

Chart showing admissions for malaria by months. 287

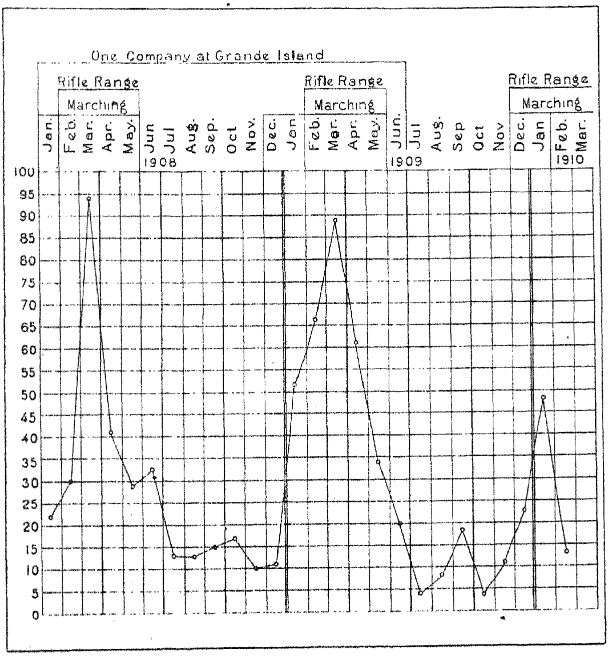

CHART SHOWING ADMISSIONS FOR MALARIA BY MONTHS.

THE INCIDENCE AND COMPLICATIONS OF MALARIA IN THE PHILIPPINE ISLANDS WITH SPECIAL REFERENCE TO ITS TREATMENT WITH ARSENOPHENYLGLYCIN.[1]

By Fred B. Bowman.

(*From the Department of Tropical Medicine, Philippine Medical School, Manila, P. I.*)

Between the years 1904 and 1908 approximately 36,700 deaths occurred in Manila. Of these, 762, or about 3 per cent, were reported to be due to malaria. Ten per cent of the deaths from malaria occurred between the ages of 1 and 5 years. The percentage is very low between 5 and 15 years; but from 15 to 30 we find recorded 50 per cent of the total number. After the age of 30 the percentage rapidly drops until 50 is reached, after which the mortality from malaria is but 1 per cent.

About 12,000 deaths are reported annually in the Philippine Islands as due to malaria, 5 per cent of the total mortality. The following statistics were obtained from a study of the histories of 100 consecutive cases admitted to St. Paul's Hospital.

Tertian malaria was found to be most common, 43 per cent of the total number of cases being infected with this parasite. Æstivo-autumnal was more frequent than quartan fever, the former constituting 37 per cent and the latter but 13 per cent of the cases.

Approximately 50 per cent of the cases had an enlarged spleen, the type of malaria seeming to influence the extent of splenic enlargement little, if at all. Two cases were sometimes seen side by side in the same ward with practically identical histories, symptoms and blood pictures; one with a spleen reaching to the umbilicus, the other with that organ not palpable.

The average red blood cell count in these cases was 3,000,000, although in a few malignant and cachectic cases it was much lower. Infection with intestinal parasites, occurring as it does in so many of the natives, to a great extent influences the blood picture, usually making differential counts of little value.

Black water fever is rare in the Philippine Islands. I have never seen a case here. Malarial dysentery is of quite common occurrence. Malaria in itself rarely is a fatal disease in these Islands, but after two years' work in the free dispensary and the wards of St. Paul's Hospital, the fact is impressed on me more and more that many of the neuroses and indefinite conditions which we meet with are due to latent malaria, or to succeeding attacks lasting over periods of years.

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 10, 1910.

The usual complications of malaria will not be dealt with in this paper, but some of the most common conditions complained of by the natives will briefly be described. The etiology of most of these appears obscure, but it may possibly in the future be cleared up in some measure by a closer questioning of the patients as to the previous diseases from which they have suffered and particularly with reference to the occurrence of "chills and fever."

A great many patients enter the free dispensary complaining of loss of sensation in the extremities which they describe as "heaviness" of the feet and legs. A large proportion of these patients are extremely anemic. The conjunctival and mucous membranes are pale, the pateller reflexes absent, and there is some loss of sensation in the extremities. Others present the typical symptoms of a peripheral neuritis. On questioning these patients carefully, a large percentage give a distinct history of recurring attacks, of chills and fever for which the Filipino has a special name, "*ñgiki.*" Too many of these cases are diagnosed as beriberi, and a great many of these diagnoses would probably be changed if the previous history of the patient were taken more thoroughly.

Nephritis among Filipinos from 15 to 30 years of age is also extremely common, and it is not unusual to see in young men perhaps five cases of chronic nephritis in a ward of twenty-five beds; not favorable cases, but those exhibiting anasarca, œdema, shortness of breath, high blood pressure and all the signs of severe kidney trouble. The etiology of a number of these cases of nephritis always has been obscure, and the great proportion of sufferers from malaria encountered, some with serious and others with moderately severe symptoms in which the urine contains albumin and casts, leads the clinician to think of the possibility that malaria is the original cause of the kidney affection.

Nearly all cases of malaria during and after the pyrexial period have larger or smaller amounts of albumin in the urine. One attack probably causes no permanent symptoms of nephritis, but repeated ones, covering periods of years, undoubtedly have a deleterious effect on the normal action of the kidneys and lead to a definite chronic nephritis; therefore, malaria should not be overlooked in studying the etiology of chronic nephritis in young adults in countries where malaria is endemic.

Many other conditions are, of course, met with in studying malaria, which from an etiologic standpoint are very indefinite, but these two complaints which I have outlined are so often recounted by the native patients, so many of whom give very indefinite histories of previous attacks of malaria, that they have been particularly discussed.

THE TREATMENT OF MALARIA WITH ARSENOPHENYLGLYCIN.

While the treatment of malaria is already on a very satisfactory basis, nevertheless, as previous experiments in the treatment of this disease with atoxyl have been reported, and as arsenophenylglycin, employed in the Biological laboratory of the Bureau of Science was giving such excellent results in the treatment of trypanosomiasis, it was decided to try the effect of this drug on malaria. Acting on the advice which was received, the drug was administered throughout in doses of 0.6 of a gram subcutaneously, a total of two or three doses being given on alternate days. The arsenophenylglycin was dissolved in 10 cubic centimeters of sterile water and immediately injected subcutaneously into the muscle of the abdominal wall or under the skin.[2]

Ten cases of malaria were treated, six of the æstivo-autumnal type, three of tertian, and one of the quartan form. The following brief excerpts are taken from the histories of the cases.

Case I.—Æstivo-autumnal malaria. Filipino man. Entered the hospital March 26, 1909. Present illness began eight months ago with pain in the legs and epigastrium. Fever occurred every other day at different periods during this time. The patient is extremely anæmic, somewhat emaciated; conjunctival and mucous membranes are extremely pale. The spleen is enlarged 3 centimeters below the costal margin and is sharp-edged and appears rather firm on palpation.

March 29: Crescents, flagellated bodies, and young forms seen in fresh blood-smear. Seventeen crescents found in counting 200 leucocytes. Urine contains albumin, but no casts. March 30: Blood-smear as before; 0.6 gram of arsenophenylglycin was dissolved in 10 cubic centimeters sterile water and injected subcutaneously into the abdominal wall. April 1: Two days later, the blood picture had not changed. Six-tenths of a gram of arsenophenylglycin given as before. April 2: Eight crescents in 200 white blood cells counted and very few young forms seen. April 3: One gram of arsenophenylglycin injected. No young forms. April 7: Numerous crescents and ovoids seen in the fresh blood-smear. April 8: An erythematous rash appeared on different parts of the body surface. April 9: The patient complains of severe pain in the stomach and cramps in the abdomen. April 12: Extreme pain in the extremities. Absence of knee jerks. The typical "steppage" gait of peripheral neuritis was evident, and later in the day severe spastic contractions of leg muscles. The administration of purgatives (calomel and magnesium sulphate) caused these symptoms to subside in a few days.

Three differential blood counts were made at different times with the following result: April 2: Polymorphonuclears, 50.4 per cent; large mononuclears, 25.6 per cent; small mononuclears, 4.7 per cent; eosinophiles, 17.5 per cent; mast cells, 0.4 per cent; transitionals, 1.4 per cent. April 5: Eosinophiles had increased to 17.5 per cent. March 29: Polymorphonuclears, 65 per cent; large mononuclears, 23 per cent; small mononuclears, 6 per cent; eosinophiles, 4 per cent; mast cells, 1 per cent; transitionals, 1 per cent. Crescent bodies could always be found in blood-smears until the patient was discharged.

Case II.—Æstivo-autumnal malaria. Filipino man. Complaint: Fever. Entered the hospital May 11. Previous illness: One year ago for two weeks he had the same trouble, with severe chills and diarrhœa. The present illness began three weeks ago with chills and fever, and severe diarrhœa.

May 11: Blood examination shows blood cells to be rather pale. Numerous crescents and a few half-grown æstivo-autumnal parasites.

May 16: Red blood cells, 5,000,000. Differential count, polymorphonuclears, 40 per cent; large mononuclears, 50 per cent; small mononuclears, 3 per cent; eosinophiles, 2 per cent; mast cells, 1 per cent; transitionals, 2 per cent.

An examination of the urine showed the presence of albumin. No casts.

May 17: Six-tenths of a gram of arsenophenylglycin given. May 18: Urine shows large quantity of albumin. May 19: Six-tenths of a gram of arsenophenylglycin given. Eosinophiles had increased to 5 per cent. May 24: Numerous crescents found and no young forms. After the last injection May 19 the temperature remained low until the patient left the hospital, but parasites were always present.

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[2] Arsenophenylglycin is rapidly oxidized in the air, the resulting product being intensely toxic.

Case III.—Tertian malaria. Filipino man. Complaint: Chills and fever for a month at first every third day, but now every day. Headache severe, and occasionally the patient says he becomes dizzy and loses consciousness. He appears extremely pale and anæmic. A hæmic murmur is heard at the base of the heart. The spleen is not enlarged and otherwise the general physical examination is negative. A blood-smear shows numerous half-grown tertian parasites.

May 26: A blood-smear is the same as above. Six-tenths of a gram of arsenophenylglycin given. May 27: No change in blood picture. May 28: Six-tenths of a gram of arsenophenylglycin given. May 30: A few half-grown forms. June 7: Severe local reaction at the site of the last injection. Later, an abscess developed which proved to be sterile.

Case IV.—Æstivo-autumnal malaria. Filipino man. Complaint: Chills and fever. Present illness has continued for three months with chills and fever two or three times a week and pains in the legs, bones and joints. The patient is very pale and weak. A soft and blowing murmur is heard at the point of maximum impulse. The spleen is enlarged 1 centimeter below the costal border.

May 27: A blood-smear shows young amœboid forms and also nearly full-grown æstivo-autumnal parasites. No crescents seen. May 28: Six-tenths of a gram of arsenophenylglycin given. May 29: No changes in the blood picture. May 30: A few crescents found and very few young forms. Six-tenths of a gram of arsenophenylglycin given. June 12: A blood-smear shows numerous crescents, no young forms. The patient has gained in weight and feels perfectly well. When he entered the hospital much albumin was found in the urine. At the time of discharge no albumin was present.

Case V.—Æstivo-autumnal malaria. Filipino man. Complaint: Chills and fever. Typical symptoms of malaria. The spleen is enlarged 10 centimeters below the costal margin; it is movable and soft.

May 20: Young intracorporeal forms and crescents present in a blood-smear. May 26: Crescents and young amœboid forms. Six-tenths of a gram of arsenophenylglycin given, the patient's temperature being 40° at the time of injection. The temperature dropped, but rose again on June 1, when 1 cubic centimeter of a solution of hydrochloride of quinine was given and then 0.62 gram three times a day until the patient was discharged on June 16, on which date a blood-smear showed a few crescents but no other forms of the parasite.

Case VI.—Tertian malaria. Filipino man. Complaint: Chills and dysentery. The patient is extremely pale, tongue coated and breath foul. A general physical examination shows nothing of importance except an enlarged liver, 3 centimeters below the costal border. The spleen is not enlarged.

May 28: Numerous tertian parasites found in the blood. May 30: Parasites found in a blood-smear. June 2: Six-tenths of a gram of arsenophenylglycin given. June 7: Marked local reaction at the site of injection. A blood-smear was negative. June 10: The abscess opened and drained. No organisms were seen in a stained smear and no odor is present. June 19: Blood examined after a slight rise in temperature, and parasites found.

Case VII.—Subtertian (malignant) malaria. Filipino man. The patient is in a semiconscious condition and will not answer questions. He is extremely anæmic; the liver is not enlarged and the spleen is not palpable. A blood-smear showed red blood cells very pale and vacuolated with poikilocytosis and anisocytosis. Numerous hyaline amœboid forms seen in the cells, sometimes two in one red blood cell. Red blood cell count, 2,500,000.

May 31: Six-tenths of a gram of arsenophenylglycin given. June 1: Hyaline bodies numerous. June 2: Hyaline bodies numerous and 0.6 gram of arsenophenylglycin given. June 3: A few hyaline bodies seen. June 5: The patient was in a semicomatose condition and a hypodermic injection of 1 cubic centimeter hydrochloride of quinine was given, when the temperature fell and the patient rapidly improved under quinine sulphate. After the injection the patient developed two severe abscesses which were sterile.

Case VIII.—Quartan malaria. Filipino woman. Complaint: Pain in the legs and abdomen. Previous illness: Ten years ago the patient had chills and fever, and was treated with quinine. Present illness: This began six months ago and the patient now complains of severe pains and tenderness in the muscles of the calves of the legs. The spleen is enlarged to 1 centimeter below the costal margin. Knee jerks are absent. A blood-smear shows numerous quartan parasites.

June 7: Six-tenths of a gram of arsenophenylglycin given. June 8: Parasites present. June 9: Half-grown and nearly mature parasites present. Severe tenderness over the sites of the injection. Six-tenths of a gram of arsenophenylglycin given. June 11: Sterile abscesses present, which on being drained quickly healed.

Case IX.—Æstivo-autumnal malaria. Filipino man. The patient is almost in a comatose condition and answers questions very unsatisfactorily. The spleen is enlarged to 2.5 centimeters below the costal margin. Numerous young forms as well as crescents were present in the blood.

June 7: Crescents numerous. Many ovoids present. Six-tenths of a gram of arsenophenylglycin injected. June 8: Tenderness over the area of injection. Crescents present. June 9: Six-tenths of a gram of arsenophenylglycin given. The temperature at the time of injection was 40° C. June 12: An abscess at the site of inoculation. Quinine, 1 gram, given hypodermically as the temperature is rising and the blood shows numerous parasites. June 16: The abscess evacuated, the pus proving to be sterile.

When the patient was discharged crescents could still be found in a blood-smear, although no young forms were seen.

Case X.—Tertian malaria. Filipino man. Present illness: Began three months ago with chills and fever. The history and examination show nothing of importance except an enlarged spleen 3 centimeters below the costal border. A blood-smear shows numerous adult tertian parasites.

June 16: Six-tenths of a gram of arsenophenylglycin given. The patient had no fever at the time of injection, which was given not on the day of the usual paroxysm. June 17: The patient had a paroxysm as usual. June 18: No temperature. Six-tenths of a gram of arsenophenylglycin given. Later in the day the patient had chills and high fever. June 19: The temperature did not return to normal. June 20: The temperature again rose. June 21: One cubic centimeter of hydrochloride of quinine given and the temperature returned to normal and remained so until the time of patient's discharge from the hospital.

All the cases treated complained of severe pain at the time of injection.

Case I, diagnosed as *æstivo-autumnal fever,* received altogether 2.2 grams of arsenophenylglycin and in five days developed symptoms of arsenical poisoning.

In some cases of æstivo-autumnal infection the young forms of the parasites seemed to disappear after injection of the drug, but in all instances the crescents were not affected.

No definite effect was noted in the three cases of tertian malaria, parasites being found in each, at some period after the injections of arsenophenylglycin. No effect was produced in the case of quartan malaria.

Severe abscesses resulted from the injections in five cases. All were sterile, no growth occurring when the pus was transferred to culture media.

The effect of the drug on the kidneys was practically negative. Case II showed some increase in the amount of albumin after treatment. On the other hand, the albuminuria disappeared in Case IV after treatment with arsenophenylglycin.

CONCLUSIONS.

1. Splenomegaly is by no means a constant symptom of malaria.
2. Chronic nephritis is a common sequel of recurring attacks of malarial fever.
3. Peripheral neuritis and many of the cases diagnosed as beriberi may be attributed to frequent previous attacks of malaria.
4. Treatment with arsenophenylglycin produces no definite effect on the life of the malarial parasite, and has seemingly no effect on the crescent body.
5. An overdose of arsenophenylglycin may produce the symptoms of arsenical poisoning.

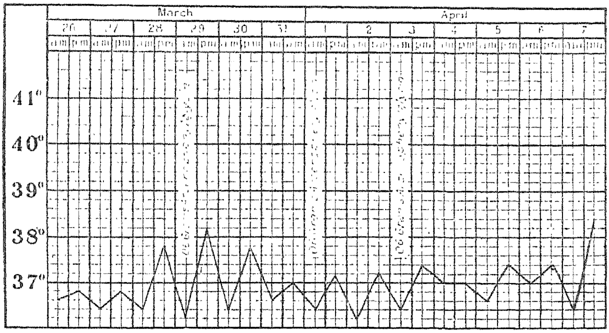
One case of filariasis was also treated with arsenophenylglycin. The patient's blood was examined at intervals of four hours for twenty-four hours; at 1.30 p. m. no embryos were found in three drops, but at 5 a. m. 50 motile organisms were present.

In all, 3 grams of arsenophenylglycin were given to this patient, who also developed symptoms of arsenical poisoning, with an erythematous rash which later went on to the stage of desquamation.

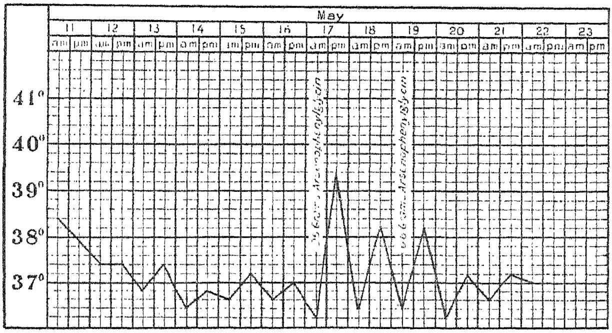
The filarial embryos were unaffected, 65 being counted in three drops of blood after the treatment.

ILLUSTRATIONS.

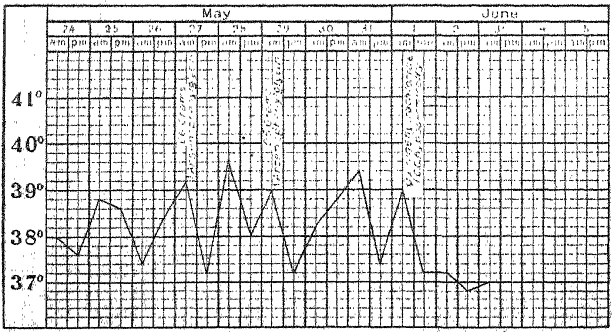
Charts 1–10.



Case No I



Case No.II



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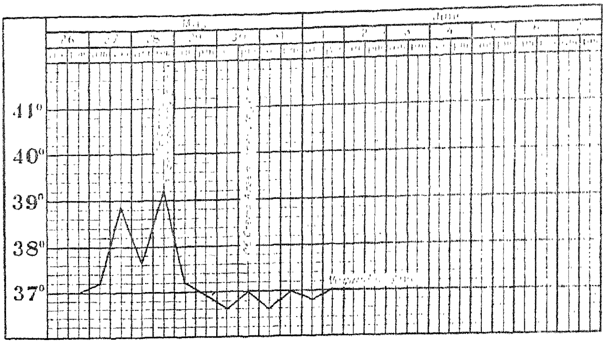

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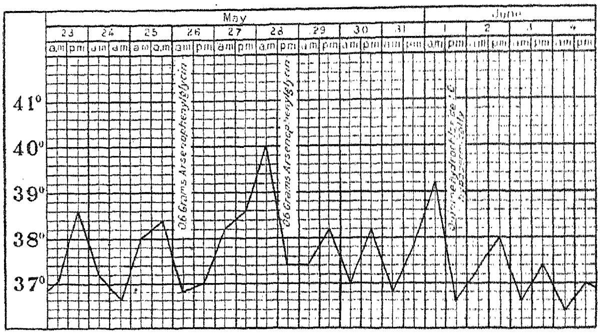
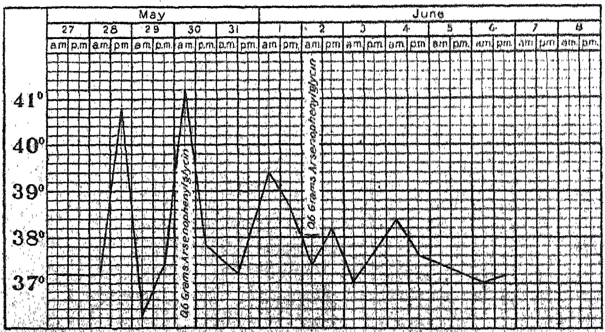
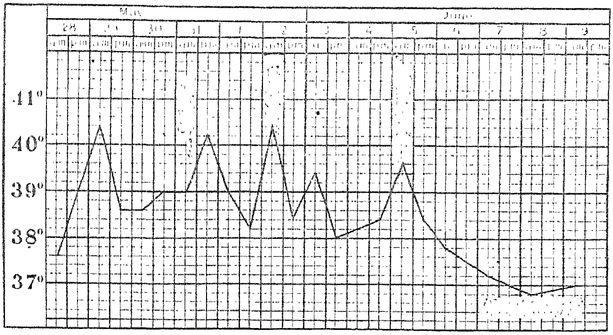


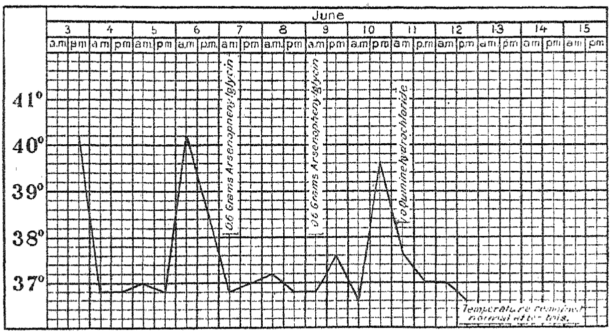
Case No.V.



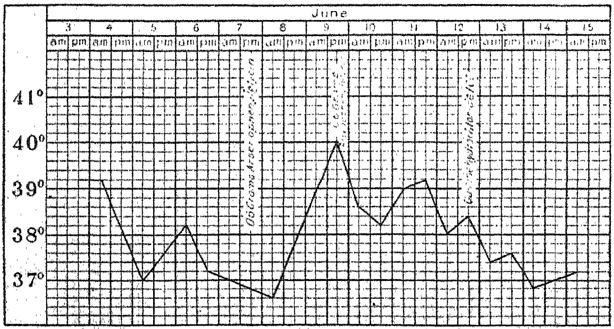
Case No.VI



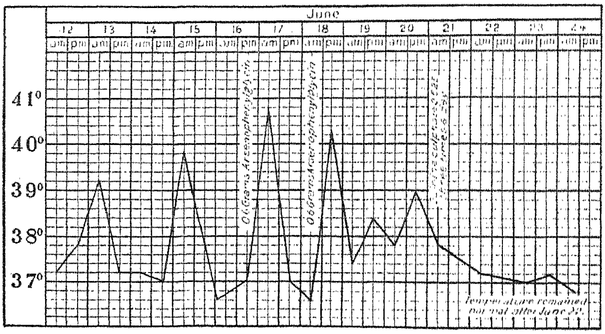
Case No.VII



Case No VIII



Case No IX


June
12
13
14
15
16
17
18
19
20
21
22
23
24
am
pm
41°
40°
39°
38°
37°
0.6 Grams Arsenophenylglycin
0.6 Grams Arsenophenylglycin
Temperature remained normal after June 24.

Case No. X

NOTES ON CONTAGIOUS OPHTHALMIA.[1]

By GILBERT E. BROOKE.[2]

The subject of contagious ophthalmia is one of considerable importance in many parts of the world, for, not only is the factor of contagion high, but the condition is one which often causes much personal discomfort, suffering or disfigurement, and entails much expense and loss to employers of native labor.

During several years' work as port health officer in Singapore, I had been frequently struck with the number of "sore eyes" which were met with among Chinese coolie immigrants, and had noticed the alarming rapidity with which conjunctivitis spreads among the contract coolies confined in depots ashore.

A visit to Hongkong, Amoy, and Swatow, in 1907, still further directed my attention to the subject of trachoma, and on seeing the stringent regulations framed by the United States to prevent the introduction of the disease into their territory I began to wonder what amount of trachoma was prevalent in the East and whether any standard of diagnosis was adapted.

Toward the end of 1908 I examined several sore eyes among incoming coolies who had no trachoma, but smear examinations showed several cases of infection by a Gram-negative organism, one by a diplo-bacillus, and one by a Gram-positive organism.

The subject seemed one of considerable interest, and I therefore had removed to the quarantine station (for diagnosis and treatment) every case of conjunctivitis found on board Chinese coolie ships during the whole of the year 1909, and also made notes of cases occurring among the Malay *lascars* of the marine department.

Some of the cases were examined in my own office laboratory and others by my resident medical officer at the quarantine station, Doctor Raltray, who has kindly put his notes at my disposal.

The immigrants for the year numbered over 240,000 and the Malay staff referred to previously, 100. Out of this material I found 137 cases of conjunctivitis. On examination these proved to be:

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 10, 1910.

[2] Port health officer, Singapore; delegate from the Straits Settlements, Singapore.

		Per cent
1. *Catarrhal:*		
Koch-Weeks bacillus	75	73.7
Gram-positive bacillus	20	
Morax-Axenfeld bacillus	6	
2. *Granular:*		
Trachoma	7	= 5.1
3. *Purulent:*		
Gonorrhœal	3	
Staphylococcal	1	
4. *Unclassified*, but not trachoma	25	
Total	137	

The subject of conjunctivitis may be divided into the following headings:

1. *Catarrhal:*
    - (*a*) Acute.
    - (*b*) Chronic.
    - (*c*) Follicular.
2. *Granular.*
3. *Purulent:*
    - (*a*) Gonorrhœal.
    - (*b*) Ophthalmia neonatorum.
4. *Membranus:*
    - (*a*) Croupous.
    - (*b*) Diptheritic.
5. *Phlyctenular.*

We need not here concern ourselves with purulent, membranous and phlyctenular conjunctivitis, for the cause and treatment is well known to all; but the catarrhal and granular types are less definite and therefore of greater interest at present.

CATARRHAL CONJUNCTIVITIS.

There are many synonyms for this affection, such as catarrhal ophthalmia, blight, sore eyes, bright eye, etc. The nomenclature is unfortunate, as many cases do not present a condition which coincides with our understanding of what constitutes a catarrh at all, but the term catarrhal conjunctivitis is still preserved in the *acute* form for want of a better one.

Etiology.—As far as work has gone at the present time, we find acute catarrhal ophthalmia to be brought about by at least three different causes: (*a*) The *Koch-Weeks* bacillus; (*b*) a Gram-positive organism; and (*c*) the *Morax-Axenfeld* bacillus. A similar etiology will also be found in the incipient stages of purulent and of granular conjunctivitis.

This latter point is of importance as showing the necessity for isolation of cases of acute conjunctivitis in the work of inspection for trachoma.

(*a*) *The Koch-Weeks bacillus.*—This bacillus was first found in Egypt by Koch in 1883, when he was examining some sore eyes. The discovery was confirmed by Kartulis of Alexandria. The organism was first cultivated by Weeks in New York in 1890. It is somewhat allied to the influenza bacillus, but differs culturally from it, in that the bacillus of influenza will not usually grow characteristically except in blood media. The Koch-Weeks bacillus grows best on serum-agar, but the growth is quite satisfactory also on nutrient-agar at 37° C. and also on glycerin agar plus ascitic fluid.

The colonies occur as transparent dots which tend to coalesce, but never attain a large size. The bacillus is 1.5 to 2 μ in length and about 0.4 μ in thickness. It forms no spores, is nonmotile and is Gram-positive. Its power of resistance is slight and therefore it seems probable that the dust-born spread of this disease will not often occur. The contagion probably is transmitted either directly by the hands, or indirectly by means of flies. In Egypt, the common house fly is probably the usual channel of infection. In Singapore I have found a very small brownish-red fly, often in large numbers, on coolie ships. I have sent home for identification specimens of this insect.

That the *Koch-Weeks* bacillus is accountable for much or our Eastern ophthalmia seems probable from the fact that it was encountered in 54.7 per cent of my series of cases.

A *second cause* of catarrhal ophthalmia is a bacillus of which I can find no reports or descriptions. It somewhat resembles the *Koch-Weeks* organism in appearance, but is slightly larger, varying from 2 to 2.5 μ in length. It is nonmotile and forms no spores. The main point of difference from the *Koch-Weeks* organism is that it is Gram-positive. The only cultures I have tried have been on nutrient agar where growth occurred fairly readily as small, dotted colonies.

Clinically, the effect of the organism much resembles that of the *Koch-Weeks* bacillus, but Doctor Raltray has remarked in several of his cases a somewhat follicular type of conjunctivitis. I hope to undertake further work on this organism, with animal inoculations and on various culture media. That the bacillus is not uncommon may be concluded from the fact that it was found in 14.6 per cent in my eye series.

The *third cause* of catarrhal ophthalmia is the *Morax-Axenfeld* bacillus.

This was first found by Morax in 1896, and independently by Axenfeld. It is about 1 to 2 μ in length and frequently occurs in pairs. It grows readily in Loeffler's blood serum which is liquefied in characteristic pits in sixteen to twenty-four hours. No growth seems to occur on agar, gelatin or the other common media. It is Gram-positive.

The bacillus has been described from Europe, Africa, North America, and Asia.

Only 4.4 per cent of the infections of my series were due to this bacillus, so that it is probably not particularly common in southern China and Malaya. Clinically, I have found this type of conjunctivitis fairly generally distributed, as in the case of the infection with the *Koch-Weeks* bacillus, but Doctor Raltray found in his cases two instances of angular conjunctivitis.

The *symptoms* of catarrhal ophthalmia call for little remark, and their severity will vary in many cases. There is intense infection of the conjunctivæ, more or less œdema of the tissues and eyelids, lachrymation and mucopurulent discharge. There is a pricking and burning feeling and photophobia in the worst cases. As a rule, the pain is slight. The lymphoid follicles may, or may not be elevated. Normally, these follicles are found scattered in the subepithelial tissue of the conjunctival reflections, and become widely developed in inflammatory conditions. If they become prominent they are then easily visible to the naked eye, but it is highly important not to mistake them for the large "sago-grain" prominences of granular ophthalmia.

All forms of catarrhal ophthalmia appear to be highly contagious. Both eyes are usually attacked, either simultaneously or within a short time after each other. If untreated, in quite a large number of cases marginal corneal ulcers occur which frequently coalesce and involve considerable areas, and this is a serious Eastern scourge.

Iritis is a less common sequela.

With regard to the *treatment* of catarrhal ophthalmia, there are several points of interest. The condition usually yields to treatment in one to two weeks, although it occasionally tends to become chronic, especially if the treatment has not properly been carried out. The essentials consist in (*a*) removing the germ by medication; (*b*) taking care of the cornea; (*c*) maintaining the patient's health.

When a case is first seen a smear should be taken for diagnosis, as this will make all the difference when choosing the drug for treatment. The cornea should be thoroughly examined and continually watched. If the specific organism proves to be the *Koch-Weeks* bacillus, I have found that silver salts give the best results in treatment. Protargol and argyrol cause less pain than silver nitrate, but their effect is not so good. As a rule I give a few drops of silver nitrate in a strength of 0.438 gram to 100 cubic centimeters of water (2 grains to the ounce). The strength should never be more than 2 per cent, or sloughing of the lids and opacities of the cornea may result. Frequent irrigations with boric acid will also be necessary to free the eyes from discharge. *No bandage should ever be used,* but the eye should be protected by a suitable shade.

A little weak oxide of mercury ointment should be applied to the margins of the lids to prevent their sticking together. If corneal ulcers occur, the treatment should be even more careful and atropine may be given. With corneal necrosis, eserin, 0.438 gram to 100 cubic centimeters of water (2 grains to the ounce) will help to stimulate the tissues. Nourishing food and tonics are indicated.

The treatment for the cases of infection with the Gram-positive organism which has been described should be on the same lines as that for an infection with a *Koch-Weeks* bacillus.

However, if the causal organism prove to be the *Morax-Axenfeld* bacillus, I have found in most of my cases that silver nitrate is worse than useless and only tends to aggravate the inflammatory condition. The treatment which usually gives the best, in fact almost specific results, is sulphate of copper in 0.25 per cent solution. The solution is best applied with a small cotton-wool mop, and the application should be less frequent as the discharge diminishes.

We now come to the subject of *granular conjunctivitis* or *trachoma*, which is sometimes known as Egyptian or military ophthalmia. This disease is of very wide distribution and frequently leads to very serious results. Its contagious character has been proved many times by inoculation experiments and in all such cases the early symptoms resemble those of catarrhal ophthalmia.

As its contagious character is well recognized, it follows almost certainly that the infecting element is a microörganism. At different times for the last fifteen years many bacilli have been described, but the correct solution has not yet been found. Several spirochætæ have been found on the conjunctival surface, but these occur in other irritative conditions and are probably only saprophytic.

During the last two years Greeff and Prowazek working independently in Germany, and a medical committee of two in Iowa, have discovered in trachomatous cells certain minute bodies now known as "trachoma bodies." It is possible that these may be the specific cause of the disease. They are slightly ovoid and smaller than any known cocci. They have been found in the contents pressed out from the follicles, in desquamated epithelial cells and in the actual tissues. They occur massed together near the cell nucleus, and appear to be encapsulated. The capsule enlarges, causing the rupture of the cell and the discharge of the granules. Whether the organism occurs in the epithelium, in the lymphoid follicles or in the fibro-adenoid layer, the resultant toxic effects are most marked in the adenoid layer of the tarsal conjunctiva and the retrotarsal folds.

The *symptoms* are usually as follows: There is a preliminary, acute congestion of the conjunctiva. Very soon small, gray spots rather smaller than a pin's head in size appear in the tarsal conjunctiva of the upper lid. These have been called by Von Graefe "primary granulations," but if there is much congestion accompanying the conjunctivitis, they may be obscured. Translucent "sago-grain" granules speedily form in the culdesac and palpebral conjunctiva. The plica semilunaris and caruncle are congested and chemosis may be present. There is intense photophobia and considerable discharge. After a week or two the acute condition passes into a chronic state, which is often highly intractable. The chief sequelæ (and these together are pathognomonic) are (*a*) corneal ulceration and pannus leading to opacity; (*b*) formation of scar tissue, leading to entropion and trichiasis; (*c*) conjunctival xerosis and shrinking.

Thus it is seen that the disease is highly contagious, very chronic and leads to grave results. It has frequently been said that trachoma is extremely common in the East. My experience with over 2,000,000 coolies, chiefly from ports of southern China, has not supported this belief. My series last year showed a percentage of only 5.1 to be trachoma. In order to check this result, I looked up the records of the general and pauper hospitals in Singapore, for several years, which disclosed the following:

Conjunctivitis.

Date.	Catarrhal and purulent.	Granular.
1903	122	Nil.
1904	68	Nil.
1905	6	Nil.
1906	229	2
1907	117	[a]21

[a] Also a high total of 14 at quarantine station.

These figures seem to support the other results.

The *modes of treatment* are multidinous.

1. The best results seem to be secured by—

(*a*) Expressing the follicles with a flat Grady's forceps or the roller forceps of Knapp. This is best done under an anæsthetic.

(*b*) Painting the ruptured surface with a little bichloride of mercury.

(*c*) After a day or two the daily application of solid sulphate of copper should be begun and continued until all traces of hypertrophy have vanished.

The various other methods of treatment have been advocated as (2) Galezowski's excision of retrotarsal folds; (3) Kuhut's removal of tarsus; (4) Merck's extract of abrin (sequiritol); (5) X rays, introduced by Mayon in 1902; (6) radium, tried by Treacher Collins in 1904.

However, none of these methods has been as successful as the first mentioned. Cases are frequently eventually cured, but seldom in less than several months, often years.

In conclusion, and to summarize the main points brought out by my series of observations:

1. The percentage of infections with the Koch-Weeks bacillus was much higher than is usually supposed to be the case.

2. A Gram-positive organism was not infrequently met with.

3. The first stage of trachoma is an acute catarrhal ophthalmia, the importance of which should not be overlooked.

4. Trachoma would seem to be somewhat more rare in southern China and Malaya than has generally been thought to be the case.

THE PRESENT POSITION OF THE LEPER IN VIEW OF THE RESOLUTIONS PASSED AT THE INTERNATIONAL CONFERENCE ON LEPROSY AT BERGEN, 1909.[1]

By Sir ALLAN PERRY.[2]

It must be confessed that very little advance in the treatment of leprosy has taken place during the twelve years' interval which has elapsed since the First International Conference of Berlin was held in 1897. All we can say is that the Second International Conference confirms the views as to the cause of leprosy, its contagious nature and the desirability of isolation and segregation; but as to its successful treatment in the way of prevention or cure, this conference has not been able to do anything except to condemn some recent hypotheses which have been circulated widely and accepted by some members of the medical profession.

Therefore, the leper is in the same position in which he was twelve years ago, which is a disappointment when we consider the large amount of research work on this disease that has been carried out during that period in nearly all countries by men of the highest scientific attainments and clinical experience.

The resolutions passed at the Second International Conference are as follows:

I. The Second International Conference on Leprosy confirms in every respect the resolutions adopted by the First International Conference of Berlin, 1897. Leprosy is a disease which is contagious from person to person, whatever may be the method by which this is effected. Every country, in whatever latitude it is situated, is within the range of possible infection by leprosy and may, therefore, usefully undertake measures to protect itself.

II. In view of the success obtained in Germany, Iceland, Norway, and Sweden, it is desirable that other countries with leprosy should proceed to isolate their lepers.

III. It is desirable that lepers should not be permitted to follow certain occupations which are particularly dangerous in respect to the contagion of leprosy. In every country and in all cases the strict isolation of the leprous beggars and vagrants is necessary.

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 8, 1910.

[2] Principal civil medical officer, Ceylon.

IV. It is desirable that the healthy children of lepers should be separated from their leprous parents as soon as possible and that these children should remain under observation.

V. An examination should be made from time to time of those who have lived with lepers, by a competent physician.

VI. All theories on the etiology and the mode of propagation of leprosy should be carefully examined to ascertain if they accord with our knowledge of the nature and the biology of the bacilus of leprosy. It is desirable that the question of the transmissibility of leprosy by insects should be elucidated, and that the possibility of the existence of leproid diseases among animals (rats) should receive early study.

VII. The clinical study of leprosy induces the belief that it is not incurable. We do not at present possess a certain remedy. It is desirable, therefore, to continue the search for a specific remedy.

For the purpose of comparison, the following are the resolutions passed at the First International Conference on Leprosy at Berlin, 1897:

I. In all countries in which leprosy occurs in foci, or is widely distributed, isolation is the best means of preventing the spread of the disease.

II. The system of compulsory notification, supervision, and isolation, as carried out in Norway, should be recommended to all nations possessing local self-government and an adequate number of physicians.

III. It must be left to the legally constituted authorities, after consultation with the sanitary authorities, to determine the special regulation which must be adapted to the special social conditions (of each country).

With regard to the resolutions passed at the Second International Conference, the original of No. II read as follows:

"In view of the success obtained in Germany, Iceland, Norway, and Sweden, it is desirable that these countries should isolate lepers, placing them under such conditions of life as can be *voluntarily accepted by them*," but the members of this conference objected to the word "voluntarily" and passed the resolution as it stands in the paragraph numbered II above.

Another great advance was made when Sir Jonathan Hutchinson proposed as an amendment to the resolutions that as the papers and discussions were presented principally in the German and French languages, with which probably many of the members of the conference were not familiar, it would be better to come to no determination, particularly with regard to that distinguished observer's ideas, as to the relation of a decomposed fish diet with the cause of this disease. This amendment was lost by a very large majority, only two members (including the proposer of the amendment) voting for it, which indicates that the fish theory is not generally accepted.

The failure to carry this amendment has cleared the way considerably for further research along new lines.

Perhaps the most important resolutions passed at the Second International Conference were the following: The second resolution, as to the absolute necessity for *isolation;* the fourth, "that the children of lepers should be separated from their parents as soon as possible and that they should remain under observation;" and the sixth, "All theories on the etiology and propagation of the disease should be carefully examined to ascertain if they accord with our knowledge of the nature and the biology of the bacillus of leprosy. It is desirable that the question of the transmissibility of leprosy by insects be elucidated, and that the possibility of the existence of leproid diseases among animals (rats) should receive early study."

The concluding paragraph of the resolutions that "we do not at present possess a certain cure" for leprosy is melancholy because of the hopes that are raised whenever a fresh treatment is suggested, which hopes thus far always have ended in disappointment. The same result has attended many "cures" vaunted by their authors in the case of other serious and widespread diseases, but it is well to recognize failure as early as possible and from the feeling expressed at this last leprosy conference it is apparent that the treatment by Doctor Dycke's "nastin" is likely to follow Captain Roost's serum into oblivion.

It was my privilege two years ago, to see some of Doctor Heiser's work in the management of leprosy in the Philippine Islands, and after attending the Bergen Conference last year I was impressed by the fact that the Government of the Philippines had anticipated the measures recommended by the members of that conference by some years.

At the conclusion of the Bergen Conference the delegates for Great Britain and her colonies passed further resolutions at an informal meeting which were to be submitted to the English Government as an indication of the lines upon which, in their opinion, the management of leprosy should be conducted. The following are the resolutions referred to and they were unanimously approved by the eight British delegates who attended the conference and are to be taken in conjunction with the official recommendations passed at the conference.

We, the undersigned delegates from the British and certain colonial governments, unanimously approve the resolutions adopted at the Second International Scientific Congress on Leprosy, held at Bergen, August 16 to 19, 1909. At a special meeting held by us on the 20th of August, 1909, we agreed to the following additional resolutions:

I. Leprosy is spread by direct and indirect contagion from persons suffering from the disease. The possibility that indirect contagion may be effected by fleas, lice, the itch parasite, etc., has to be borne in mind. Leprosy is most prevalent under conditions of personal and domestic uncleanliness and overcrowding, especially where there is close and protracted association between the leprous and nonleprous.

II. Leprosy is not due to the eating of any particular food, such as fish.

III. There is no evidence that leprosy is hereditary; the occurrence of several cases in a single family is due to the contagion.

IV. In leprosy, an interval of years may elapse between infection and the first recognized appearance of disease. It is a disease of long duration, though some of its symptoms may be quiescent for a considerable period and then recur.

V. The danger of infection from leprous persons is greater when there is discharge from mucous membranes, or from ulcerated surfaces.

VI. Compulsory notification of every case of leprosy should be enforced.

VII. The most important administrative measure is to separate the leprous from the nonleprous by segregation in settlements or asylums.

VIII. In settlements, home life may be permitted under regulation by the responsible authorities.

IX. The preceding recommendations, if carried out, will provide the most efficient means of mitigating the leper's suffering and of assisting in his recovery, while at the same time they will produce a reduction and ultimate extinction of the disease.

TUBERCULOSIS AMONG FILIPINOS. A STUDY OF ONE THOUSAND CASES OF PHTHISIS.[1]

By W. E. Musgrave and A. G. Sison.

(From the Department of Clinical Medicine, Philippine Medical School, Manila, P. I.)

The present status of the tuberculosis problem in the Philippine Islands may be summed up in one sentence: A remarkably high incidence, unusually favorable conditions for the spread of the disease, and an almost complete absence of organized effort to combat it. It may be stated in general that conditions favorable for the spread of tuberculosis are practically perfect in this Archipelago. Overcrowding in unsanitary houses located too close together in unsanitary places and closed at night is all but universally prevalent. Our records show many instance of from six to ten or more people living and sleeping in a single room with from one to several individuals among them suffering from advanced pulmonary tuberculosis. Children are born and reared under these circumstances and very frequently nursed by their tubercular mothers.

The dormitories of many of the schools contain tubercular patients to a startling degree. We have records of dormitories in which fifteen to twenty students are sleeping in the same room, with two or more of them suffering from fairly advanced phthisis. Even in our public schools, tubercular patients are often found mingling with other pupils in too close contact for the safety of the whole.

The disease is very prevalent among all classes of people whose occupations are such as to keep them in close relationship with healthy persons. In this class may be mentioned street car conductors and motormen, carriage drivers, house servants, cooks and nurses of infants. During the last year we have caused the dismissal of no less than fifteen women suffering from phthisis who were caring for and in some instances sleeping in the same rooms with the children of their employers. The particular dangers from promiscuous coughing and expectoration are unknown to the majority of the patients, and these acts are practiced unrestrictedly at all times and in all places.

Poor food and lack of exercise are very potent predisposing factors to tuberculosis among the poor of these Islands. The influence of food poor in fats and proteins and excessively rich in carbohydrates is shown by the very marked improvement which so often follows the administration to tubercular patients of good food or cod liver oil. The average Filipino of the poorer class has a peculiar manner of breathing with but slight chest motion, and the vast majority not only have no conception of how to expand the chest but it is often very difficult to induce individuals to do so under instruction.

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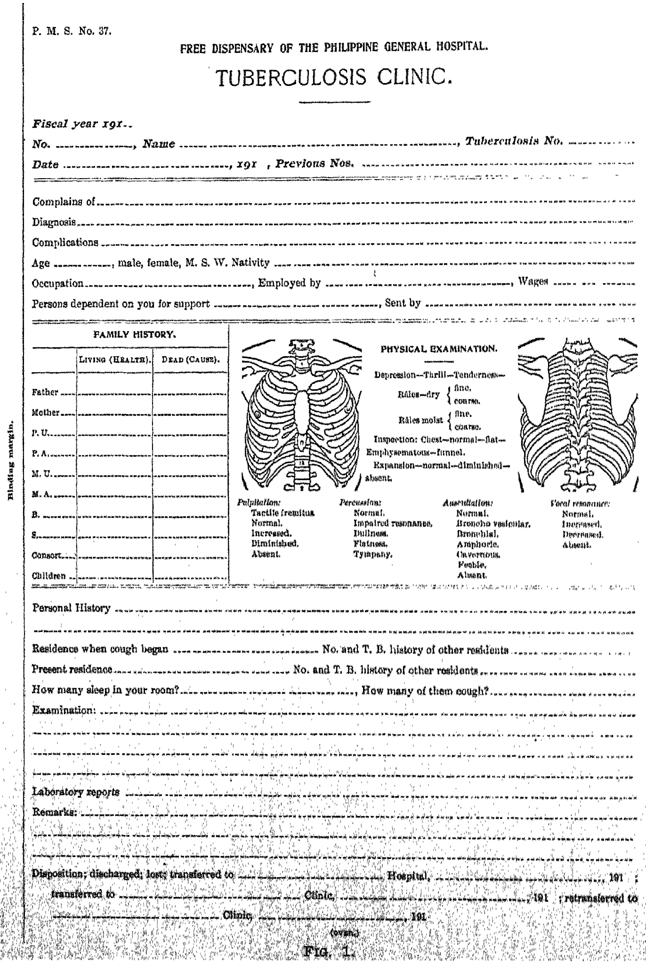
[1] **Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 12, 1910.**

The tuberculosis clinic of the Free Dispensary of the Philippine General Hospital is the first clinic specially for tuberculosis to be established in the Philippine Islands.

It has been in operation for nine months, and of the 1,047 people who have applied for treatment, 914 were suffering from phthisis and their records are tabulated in this paper. The system used in the clinic is very similar to that in operation in many countries. At the first visit a careful history is obtained and a complete examination of the patient is made and recorded on a suitable blank form (see figs. 1 and 2).



P. M. S. No. 37.

FREE DISPENSARY OF THE PHILIPPINE GENERAL HOSPITAL.

TUBERCULOSIS CLINIC.

Fiscal year 191..

No. ...., *Name* ...., *Tuberculosis No.* ....

Date ...., *191* , *Previous Nos.* ....

Complains of ....

Diagnosis ....

Complications ....

Age ...., male, female, M. S. W. Nativity ....

Occupation ...., Employed by ...., Wages ....

Persons dependent on you for support ...., Sent by ....

FAMILY HISTORY.

	LIVING (HEALTH).	DEAD (CAUSE).
Father		
Mother		
P. U.		
P. A.		
M. U.		
M. A.		
B.		
S.		
Consort		
Children		

PHYSICAL EXAMINATION.

Depression—Thrill—Tenderness—

Râles—dry { fine. coarse.

Râles moist { fine. coarse.

Inspection: Chest—normal—flat—Emphysematous—funnel.

Expansion—normal—diminished—absent.

Palpitation:	*Percussion:*	*Auscultation:*	*Vocal resonance:*
Tactile fremitus	Normal.	Normal.	Normal.
Normal.	Impaired resonance.	Broncho vesicular.	Increased.
Increased.	Dullness.	Bronchial.	Decreased.
Diminished.	Flatness.	Amphoric.	Absent.
Absent.	Tympany.	Cavernous.	
		Feeble.	
		Absent.	

Binding margin.

Personal History ....

Residence when cough began .... No. and T. B. history of other residents ....

Present residence .... No. and T. B. history of other residents ....

How many sleep in your room? ...., How many of them cough? ....

Examination: ....

Laboratory reports ....

Remarks: ....

Disposition; discharged; lost; transferred to .... Hospital, ..., 191 ;
transferred to .... Clinic, ..., 191 ; retransferred to .... Clinic, ..., 191

(over.)

FIG. 1.

DATE.	PHYSICIAN.	TREATMENT.	WEIGHT.	REMARKS.

Binding margin.

FIG. 2.

Patients are required to report once a week for subsequent observation, and at these visits they are weighed, questioned as to the progress of the disease and occasionally reëxamined. When a case is completed by death, recovery, a long period of absence from the clinic, or in any other manner, the record is closed, and as sufficient numbers of such records are completed they are indexed and bound and become a part of the general record system of the hospital.

The records of this clinic, together with certain other statistics which we shall use in the discussion, while not large enough to be conclusive, point to some rather remarkable conditions in our local problem of tuberculosis.

INCIDENCE.

The available statistics indicate a very high prevalence of the disease. Over 20 per cent of all patients applying for treatment at St. Paul's Hospital have phthisis and hundreds of advanced cases of this disease are refused admission to that institution every month. In 100 consecutive autopsies in the Malecon Morgue, Gilman[2] reported about 40 per cent as having active tubercular lesions, and Andrews, in 500 similar autopsies, encountered about 32 per cent. The 914 cases of phthisis considered here represent 22 per cent of all patients applying at the out-patient department of the Philippine General Hospital during the nine months covered by the record. This record, outlined by city districts, is shown in the following table, which also shows the very general distribution of the patients applying for treatment.

TABLE I.—*Showing residence.*

Districts of the city.	Number at all clinics.	Number at tuberculosis clinic.
Tondo	456	106
Binondo	372	81
Trozo	117	36
Quiapo	194	43
Santa Cruz	98	130
San Miguel	142	25
Sampaloc	172	33
Santa Mesa	89	18
Santa Ana	37	15
Paco	354	85
Pandacan	61	11
Malate	337	59
Ermita	129	15
Intramuros	647	101
Provinces	820	156

The family history (Table II) of the 914 cases shows a prevalence of family tuberculosis which is, so far as we have found, not equaled by any other report in the literature of the subject. The data have been carefully obtained and minimize rather than exaggerate the actual conditions. In particular, the percentage of infection among the children probably is much below the actual condition because of the total mortality of the infants (59 per cent), the majority die during the first year of life and no doubt in many instances before tuberculosis has been contracted or has developed to a degree sufficient for recognition.

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[2] *This Journal, Sec. B* (*1908*), 3, 211.

TABLE II.—*Showing family history.*[a]

Family.	Total number.	Number living.	Number dead.	Number tubercular.	Per cent tubercular.
Father	914	256	258	169	18
Mother	914	327	537	272	29
Paternal uncles	466	165	301	155	33
Paternal aunts	318	98	220	104	32
Maternal uncles	401	126	295	135	33
Maternal aunts	465	155	310	161	34
Brothers	2,094	937	1,157	167	7
Sisters	1,866	914	952	135	7
Consort	601	443	158	104	17
Children	1,920	887	1,023	83	4

[a] Family history positive in 88 per cent of all cases.

Our findings as to the infection with tuberculosis in *ascendants* as compared with those of three other authors are shown in the following table:

TABLE III.—*Showing tuberculosis in ascendants.*

	Williams.	Solly.	Osler.	Manila.
Total cases	1,000	250	427	914
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*
Parental	12	28	24	47
Collateral	34	19	----------	35

Contact, other than that naturally encountered in the study of the disease in ascendants and descendants, shows as a strong factor in the etiology. Unfortunately, our early records are not complete in this respect, but from the data which have been secured in a smaller number of cases, actual contact in residence and mostly to the extent of sleeping in the same room with tubercular patients for a greater or lesser length of time, will exceed 70 per cent of all cases.

Age, sex, and social condition are shown in the following table:

TABLE IV.—*Showing age, sex, and social condition.*

Ages by years.	Male.	Female.	Total.	Laborer.	Student.	Upper class.
1 to 10		1	1			
10 to 20	119	51	170	100	68	
21 to 30	185	138	323	289	23	27
31 to 40	109	88	197	194		
41 to 50	70	58	128	124		
51 to 60	43	18	61	58		
61 to 70	25	7	32	30		
71 to 80	2		2	1		
Totals	553	361	914	796	91	27

The small number of children is accounted for by the fact that these patients are cared for in another clinic. The majority of the cases of infection are seen during the second, third, and fourth decades, with a considerable number in the fifth and sixth decades. The ages are somewhat greater than the average found in many clinics, a condition which may be explained by the more generally chronic character of the disease in the Tropics.

The social condition of the patients does not give data of any considerable importance, as the majority of the cases belong to the lower classes, who are very similar in habits and customs.

Occupation is shown in the following table:

TABLE V.—*Showing occupation.*

Occupation.	Male.	Female.
Laborer	372	334
Cigar maker	24	18
Carpenter	24	
Painter	7	
Student	85	6
Government employee	29	
Cook	16	1
Servant	16	2
Totals	573	361

Ninety-one of the patients were students, 29 Government employees, 17 cooks, and 18 servants. The last are particularly interesting, because by vocation they must of necessity for a considerable part of the day be placed in rather close contact with persons whose lives are particularly valuable. During the past year six students of the Philippine Medical School were found to be suffering from phthisis.

Weights, according to ages, are shown in the following tables, but they are not of much value for comparative purposes because there are no similar tables referring to healthy Filipinos which may be used as standards.

TABLE VI.—*Showing weight according to age (male).*

Weight (kilograms).	Age.							
	10–15.	16–20.	21–25.	26–30.	31–40.	41–50.	51–60.	61–70.
22.7 to 27.2		1			1			
27.7 to 31.8	2	2	5		1	2	1	1
32.2 to 36.3		5	11	2	4	3	1	1
36.7 to 40.8		22	9	15	15	14	7	4
41.3 to 45.4	4	59	45	38	32	17	11	6
45.8 to 49.9	1	29	36	21	31	14	7	6
50.4 to 54.5		9	21	7	14	6	6	4
54.9 to 59.0		3	5	5	5	4	3	1
59.4 to 63.6			2	1	1	1		
Over 63.6					2			

TABLE VII.—*Showing weight according to age (female).*

Weight (kilograms).	Age.							
	10–15.	16–20.	21–25.	26–30.	31–40.	41–50.	51–60.	61–70.
22.7 to 27.2			2	1	1		2	
27.7 to 31.8		1	3	3	8	4	4	1
32.2 to 36.3	2	4	8	18	26	20	7	2
36.7 to 40.8	2	14	20	34	21	15	6	1
41.3 to 45.4	2	9	19	14	19	10	3	1
45.8 to 49.9		6	5	3	16	4	4	
50.4 to 54.5		4	1	4	6	2	1	
54.9 to 59.0			1		2			1
59.4 to 63.6		1			1			
Over 63.6			2					

The location of the lesions is shown in the following table, which is self-explanatory.

TABLE VIII.—*Showing location of lesions.*

	Right side.	Left side.	Both.
Apex	393	232	343
Front	299	209	306
Back	256	110	144
Base	20	11	6
Axillary	39	21	5

The stage of the disease is shown in Table IX. In this connection we have used only the simple classification of incipient, moderate, and advanced tuberculosis, because it has seemed to us that time could be better spent than in making a more elaborate classification.

TABLE IX.—*Showing degree of the disease.*

Advanced.	Moderate.	Incipient.	Total.
72	708	134	914

The duration of the disease is outlined in Table X, and the data given are based upon the patient's statements of the beginning of symptoms. For this reason the record is not very accurate, showing, of course, in many instances a much shorter duration than that which actually existed. However, when this table is considered in connection with the ages of the patients and the stage of the disease, at the time of examination it seems that the course of the infection is, as a rule, exceedingly chronic, more so, perhaps, than that encountered in temperate climates.

TABLE X.—*Showing duration of the disease.*

Duration.	Male.	Female.
Less than 1 month	84	54
1 month to 6 months	195	136
6 months to 1 year	109	72
1 year to 2 years	63	53
2 years to 3 years	47	17
3 years to 5 years	24	14
5 years to 10 years	31	15
Total	553	561

The principal subjective symptoms of these cases are outlined in Table XI. The table is self-explanatory.

TABLE XI.—*Showing principal symptoms (914 cases).*

Symptoms.	Number.
Cough	914
Bloody expectorations	469
Hemoptysis	51
Fever	673
Pain, chest	526
Pain, back	267
Sore throat and hoarseness	45
General debility	145
Gastric disturbance	48
Chest oppression	64
Night sweats	680
Palpitation	7
Dyspnœa	64
Headache	55
Insomnia	147
Chill	117
Dizziness	16

The principal complications, both tubercular and nontubercular, are shown in Table XII. The most noticeable feature of this table is the small number and variety of tubercular complications present. The unusual preponderance of phthisis over other forms of tuberculosis has been noted before this in a general way in Manila, but so far as we know, this table gives the first actual statistics of this condition.

TABLE XII.—*Showing principal complications (total, 914).*

Complications.	Tubercular.	Nontubercular.
Pleurisy, fibrinous with effusion	81	
Laryngitis	45	
Pericarditis	8	
Lymphadenitis	10	
Cystitis	5	
Pyelonephritis	2	
Scoliosis	7	
Kyphosis	2	
Asthenia	15	
Pyæmia	2	
Cardiac symptoms		16
Exophthalmia		2
Epilepsy		1
Constipation		15
Gastric symptoms		45

If the facts established in this series of cases may be accepted as an index of a general condition among the Filipino people, our local problem of tuberculosis should receive prompt and serious consideration. At first glance the great prevalence of the disease, together with the peculiar social and economic conditions obtaining among the inhabitants, would seem to produce a problem of such magnitude as to preclude the possibility of its solution. However, there is a brighter side to the picture, and it is our opinion that even without financial aid from outside sources, it is possible in Manila to make the greatest showing in antituberculosis work that the world has ever seen. The reason for this assertion is that we do not need to spend millions of dollars in clothing, housing, and otherwise preparing our patients to withstand the rigors of the winters of the temperate climates. Climate is not by any means as important a factor in the prevention and treatment of tuberculosis as it once was thought to be. What we need most is education, more room in which to breathe, and an abundance of good food and exercise. As to education, teachers are here in sufficient numbers; there certainly is an abundance of land to provide more space; exercise is free, but the food may need to be supplied until such time as the people are taught to work for it, the best form of exercise.

We do not require expensive concrete hospitals for the treatment of phthisis in the Tropics. The bamboo hut in which a family in Tondo is living may be an ideal house. What should be done is to move that house out on the Pasay beach, or anywhere else where there will be ample room, use its doors and windows for firewood, and reduce the occupants to a sensible number.

In a recent paper read before the Manila Medical Society,[3] we stated in part as follows:

> With our more or less limited funds and the peculiar local conditions modifying our problems, its solution along the usual lines of the employment of sanatoriums and other methods which must take a winter climate into consideration, is neither practical nor advisable. The continuous summer, the abundance of cheap and available real estate and the cheapness of residence construction makes large tenement houses unnecessary. In a city in the United States or Europe real estate is of such great value that reasonble air space for its tuberculous poor may be obtained only at enormous expense, while here there are thousands of hectares of cheap land in and near all cities, the cost of construction of very satisfactory buildings is exceedingly small, and, finally, the art of building houses from bamboo is a common inheritance of the people.
>
> The construction of sanatoriums of the colony type for the control of tuberculosis is not a new idea and has been carried out more or less extensively in Europe and in the United States for some years; but in these countries the expense of construction and of real estate has made it too expensive of application on a large scale in congested centers.
>
> The Philippine Islands seem to be peculiarly well adapted to colonization along very economical lines, and we, therefore, recommend the adoption of the method of the elective colony sanatorium together with the immediate construction of an experimental colony in or near Manila, and hereby submit a tentative set of plans for such a colony which have been prepared for us by Mr. C. A. Barretto, of the Bureau of Public Works.
>
> If, as we believe it will, this colony proves itself successful, the plan is economical enough to allow of its extension throughout the Islands.
>
> In general, we would say that the colony should be built and maintained under the direction of the Government. The expense of construction should be light, the Government furnishing the land, building material (bamboo and nipa), and the tenants constructing their own houses according to plans furnished them; the necessary streets and public buildings, such as hospital, schoolhouses, and residence for officials, being constructed by the Government.
>
> The operation of such a colony need not add additional expense to the budget, for officials of the Bureau of Education, Bureau of Health, and Medical School could care for the respective departments with less effort than is now being expended by them in caring for the same tuberculous people scattered here and there in their homes and in Government clinics.
>
> With an abundance of land lying idle, cheap building material, and a class of patients who are able and willing to build their own homes, the cost of construction of an experimental colony to accommodate 250 persons should be small, and we feel confident that the expense of maintenance would be less than the sum which the Government is now paying for the care of a few of its tubercular citizens. At the International Congress of Tuberculosis which met in Washington this year, Doctor Jacobs made a preliminary report of what he termed a "Farm Colony" established in connection with the Maryland Hospital for Consumptives, in which he stated that the colony was practically self-supporting after one year.

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[3] *Bull. Manila Med. Soc.* (1910), 1, 6.

This, too, notwithstanding the fact that the authorities pay the patients for their work by furnishing them free board and lodging and in some cases as much as $12 per month in addition.

The farm or "truck-gardening" idea might well be carried out here in connection with the colony, or the idea might be carried further and the patients encouraged to learn and even taught other suitable occupations, with due regard to their physical condition.

In discussing with various persons interested in the subject, the plan outlined in the paper which has been quoted, the query has been raised as to the possibility of securing a sufficient number of patients who would voluntarily avail themselves of its benefits. With this end in view we have inquired of a large number of those visiting our clinic at St. Paul's Hospital, and in every instance the patients have stated that they would gladly build their houses according to our plans and live according to our rules, provided the land and materials for construction were furnished them. From investigation we feel confident that we can give the names and addresses of enough applicants to fill the experimental colony as planned, after twenty-four hours' notice.

ORGANIZATION.

However, no one method will meet the requirements for a successful antituberculosis campaign in this or any other country. In the language of Sir William Osler: "Tuberculosis is the most universal scourge of the human race." Its problem is a general one which has proved too great for boards of public health in governments controlling subjects with much less tuberculosis and much more money than we can ever hope to have available in these Islands. The first step, and one absolutely essential for a successful local campaign, is the organization along broad lines of a National Antituberculosis Society, similar to those now operating in the majority of civilized countries. The preliminary steps to create such an organization have already been taken. At the request of the Director of Health, the council of the Manila Medical Society has appointed a committee to draw up a tentative plan of organization which is to be submitted to a general citizen's committee who will effect a permanent society. This association has also named a special committee for the same purpose, and a Philippine Antituberculosis Society is certain to follow. The idea of the committee is that the organization should be a very comprehensive one, with the usual officers and as nearly a universal membership as is possible.

The work may be outlined and divided among a number of committees such as an executive committee, a committee on ways and means, one on publicity, another on scientific work, a third on prophylaxis, a fourth on treatment, a committee on statistics, legislation, education, antispitting, and many others.

We are sure to have such an organization, we will have it at once, and, what is more important, it will be a success.

BLOOD PRESSURE IN THE TROPICS. A PRELIMINARY REPORT.[1]

By W. E. MUSGRAVE and A. G. SISON.

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Statements suggesting that the lowered blood pressure found in this climate may be considered as one of the etiologic factors in tropical pathology are scattered here and there throughout the literature of tropical medicine, but so far we have been unable to find any published observations showing that blood pressure really is influenced by tropical environment.

We are fully aware of the difficulties in the way of accurately determining what part of any variation may be peculiar to local conditions, as well as to the danger of conclusions which may be drawn from a small series of records. However, the results in the cases so far studied have been so striking that they are offered for discussion and criticism.

All of the cases are healthy adults from 25 to 40 years of age, and for the sake of convenience have been divided into the following three groups:

(*a*) Ninety-seven foreigners, who are for the greater part Americans from the Philippine Civil Service and officers and soldiers of the United States Army serving in the Philippines.

(*b*) Forty Filipinos, largely selected from the student class and from the local police forces.

(*c*) Ten French Sisters of Charity.

Although both systolic and diastolic readings, and, in many cases, tracings have been made, only the systolic records are used in this report. All the determinations have been made with the same Erlanger instrument; the readings have been made by the same persons and, in most instances, the examination has been repeated at least once.

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held in Manila, March 12, 1910.

The important results of the findings are shown by the following tables:

TABLE I.—*Systolic blood pressure of ninety-seven foreigners in Manila, showing influence of duration of tropical residence.*

Residence in Tropics.	Systolic pressure.							Total number of cases.	Average pressure.
	90-100.	101-110.	111-120.	121-130.	131-140.	141-150.	151-160.		
1 month to 1 year	1	10	15	18	12	7	2	65	124+
1 year to 5 years		4	8	2	1			15	115
5 years to 10 years			7	1				8	116+
Over 10 years		3	4	2				9	113+
Totals	1	17	34	23	13	7	2	97	

TABLE II.—*Systolic blood pressure of 49 Filipinos.*

Sex.	Systolic pressure.					Total number of cases.	Average pressure.
	90-100	101-110	111-120	121-130	131-140		
Male	9	8	8	5		30	108
Female	4	3	5	5	2	19	113
Totals	13	11	13	10	2	49	109

TABLE III.—*Systolic pressure of 10 French Sisters of Charity (24 to 38 years of age), according to tropical residence.*

Residence in Tropics.	Individual readings.	Average.
15 days to 1 year	140, 128, 114, 125	127
1 year to 5 years	115, 110, 110	112
Over 5 years	110, 106, 114	110

TABLE IV.—*Systolic pressure of 140 people of all classes, according to age.*

Age.	Systolic pressure.							Total number of cases.	Average pressure.
	90-100.	101-110.	111-120.	121-130.	131-140.	141-150.	151-160.		
15 years to 20 years	4	1	5	7	3			20	117
21 years to 25 years	7	13	14	6	5	5	1	56	104
26 years to 30 years	2	4	11	8	1	2		28	125
31 years to 35 years		3	4	3	1	1	1	13	122
36 years to 40 years		7	4	4	2			17	115
41 years to 45 years				1	1			2	130
46 years to 50 years					2			2	135
51 years to 55 years			1					1	
56 years to 65 years					1			1	
Totals	13	28	39	34	16	8	2	140	

DISCUSSION.

If the figures shown in this report should, after more extensive work, prove to be representative facts, two very important points immediately suggest themselves for solution: (*a*) The cause or causes for this very decided decrease in blood pressure in the Tropics; and (*b*) its significance in tropical pathology.

At the present time, our understanding of the physics and physiology of normal blood pressure in general is too incomplete to allow the use of available data as premises for the explanation of the phenomena of lowered blood pressure in warm countries.

The *energy of the heart,* the *peripheral resistance,* the *elasticity of the arterial walls,* and the *volume* of the *circulating blood* are the four chief factors generally accepted as the principal forces governing the normal blood pressure. All these factors are subject to considerable individual physiologic variation, and, what is more important, as well as more difficult to measure in instituting comparisons, they are so closely connected and interdependent through vasomotor and other nervous influences that changes in one may produce marked secondary effects in the others.

However, in analyzing these four major factors which influence blood pressure with the view of securing an explanation of the lowered tension in the Tropics, it seems probable that the influence of the *energy of the heart* and of the *elasticity of the blood vessels* may be eliminated. While heart and arterial diseases are sufficiently prevalent in the Tropics, all our work in the clinics and autopsy room are against the conclusion that these organs are factors in the general tendency toward lowered arterial tension.

The *volume and viscosity* of the blood have not been studied sufficiently in Manila and we are not familiar with reliable observations upon these factors in other parts of the Tropics. This important subject should be investigated carefully. The literature of tropical medicine seems to support the general opinion that anæmia is almost universally prevalent among people who have lived for some years in the Tropics; but this is by no means proved.

The clinical appearances of pallor of the skin and mucous membranes which are so prevalent are probably responsible for this opinion, but such observations do not necessarily prove that anæmia is actually present. These appearances may be explained in other ways, and work on the blood does not support the conclusions of any such general prevalence of anæmia. The estimation of hæmaglobin by *percentage* methods shows an average which will compare favorably with that of temperate climates and the number of erythrocytes per cubic millimeter of blood will show an equally normal average.

The *volume* determinations of these two points have not, so far as we know, been made on any large series of people in the Tropics, and any opinion as to the presence or absence of anæmia as determined by these methods at the present time would be speculative.

However, to judge from the data which are available, it is much more logical to explain the clinical anæmia as being due to diminished peripheral resistance and lack of the demand for a supply of blood to furnish heat to the skin than it is to assume the condition to be one of true anæmia dependent upon the greater concentration and diminished volume of blood, with a concomitant decrease in actual amount of hæmoglobin and in the total number of red blood cells.

The hypothesis offered in this paper that the anæmia is a *clinical one only* is borne out by its very evanescent character, for when patients, particularly children, in whom it is shown most markedly, are transferred to a cooler climate which requires a greater volume of cutaneous circulation, and which also increases the vasomotor tone, the *clinical* anæmia disappears with a rapidity which argues against the supposition that it is due to an actual poverty of the blood. Children who appear to be anæmic not infrequently develop normally tinted skins and mucous membranes within a very few days after having started on an ocean voyage or even after having been transported to the cooler climate of Baguio.

PERIPHERAL RESISTANCE.

Alterations in peripheral resistance as a direct result of the greater and continuous heat of the Tropics offer an attractive hypothesis for the explanation of lowered blood pressure in this climate and the confirmation of such an hypothesis would greatly simplify the study of the etiology of that exceedingly prevalent condition, *tropical neurasthenia,* as well as that of several other generally prevalent tropical clinical entities which usually are considered to be of climatic origin.

The preponderating influence of peripheral resistance in maintaining blood pressure is a proved fact. Unless some counterbalancing change in the force of the heart occurs, increased resistance raises the pressure and decreased resistance is followed by a lowering of the pressure.

Claude Bernard established a vasomotor influence over peripheral resistance, and it is now known that this resistance, both arterial and venous, is largely under vasomotor control and that the vasoconstrictor fibers are those which are principally concerned in this phenomenon. Furthermore, vasomotor tone, in particular of vascular areas, constantly varies in response to *local* needs; increased function always being accompanied by increased blood flow. If such an area be of sufficient extent and the increase is not compensated for by vasoconstriction in other vascular locations, a fall in mean aortic blood pressure follows. The most striking example of this condition is found in the great influences which the abdominal vessels, enervated by the splanchnic nerves, may exert upon the general blood pressure.

Vasomotor tone is influenced by a number of known agencies and it is often markedly affected by reflexes of remote origin, which often may not be determined in a given case.

Insomnia is often associated with hypertension, and the opposite condition usually prevails during somnolence. Certain conditions of what may be called the *higher neuroses* are accompanied by increased blood pressure, while certain forms of neurasthenia show a hypotension.

Cutaneous and other peripheral vasoconstriction and increased pressure due to cold, as well as the opposite condition due to heat, are recognized facts which suggest a probable influence of this nature in the etiology of the lowered pressure in the Tropics.

It does not seem improbable that this lowered pressure might be explained by lowered peripheral resistance in two ways. While the secretory function of the skin is increased in the Tropics, it is doubtful if this is at the expense of increased resistance, in fact, logically quite the contrary may be expected, and the normal surface resistance and vasomotor tension necessary to produce the required surface heat of temperate climates, in the Tropics is greatly diminished the year around, and in certain seasons is reduced almost to nil. This decreased vasomotor tone may logically be expected to lead to the opposite condition, or to one of stasis which could explain not only some of the variations in mean systolic pressure, but might equally explain the condition of clinical anæmia mentioned above, as well as some of the neurasthenias, cerebral anæmias, and acute œdemas of dependent portions of the body which are so prevalent in the Tropics. Another factor which must be taken into consideration is the possibility of splanchnic influences. When we remember the enormous influence which the splanchnic vasomotor tone has upon the general blood pressure, and particularly upon the portal circulation, and also that it is a proved fact that abdominal pressure has a marked influence on the general mean aortic tension, the "tropical liver" and the very prevalent sensation of abdominal vacuity which are partially responsible for the very general tropical custom of abdominal binders may have some scientific foundation.

Gastrointestinal disturbances with secondary clinical manifestations are exceedingly prevalent in this country and it is but reasonable to suppose that these conditions may produce vasomotor disturbances of sufficient magnitude to exert some influence upon the general blood pressure, principally through the portal circulation and splanchnic tone.

In conclusion, we again wish to state that much of the discussion in this paper is hypothetical and offered simply to call attention to the possibilities of continued research in an extremely interesting field in the study of medicine in the Tropics.

TUBERCULOSIS IN THE PHILIPPINE ISLANDS.[1]

By ISAAC W. BREWER.[2]

Tuberculosis is probably the most important disease which is encountered in tropical countries. In the Philippine Islands it is one of the most frequent causes of death. From the statistics gathered during the medical survey of the town of Taytay, Nichols[3] came to the conclusion that 1 per cent of the inhabitants had the disease. The statistics for 30 provinces for the year 1907, representing a population of over 4,000,000 persons, showed a death rate of 210.9 per 100,000. This is surely less than the actual rate, for only well-marked cases of phthisis are recorded as tuberculosis by the town secretary, the layman who issues the death certificates.

The following shows the death rate in the Philippine Islands for the year 1907, compared with the rates in other countries.

Death rate per 100,000, from pulmonary tuberculosis.

	Death rate.
Ireland	218.5
Philippine Islands, excluding Manila, 1907	210.9
Norway	200.4
Switzerland	190.7
Germany	181.9
United States, registration area	172.3
Scotland	150.1
Spain	144.3
The Netherlands	138.8
Belgium	127.7
England and Wales	125.7
Italy	117.0

Excepting for the Philippine Islands, the above statistics are for the five years from 1901 to 1905.

In Manila, where the vital statistics are much more accurate, there were, during the year 1908, 10,646 deaths from all causes. Of these, 1,240, or 11.07 per cent, were due to tuberculosis, a death rate of 554.2 per 100,000. During the five years ending with 1908, there were in Manila 5,373 deaths from pulmonary tuberculosis, a death rate of 485.3 per 100,000. During the same period, there were 4,472 deaths from bronchitis, a death rate of 404 per 100,000. Without doubt some of these cases of bronchitis were tubercular.

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 12, 1910.

[2] Medical Reserve Corps, United States Army.

[3] *This Journal, Sec. B* (1909), 3, 279.

The following shows the death rate from pulmonary tuberculosis in Manila and certain cities of the United States having approximately the same population. These data are for the year 1908.

	Death rate.
Manila, Philippine Islands	486.2
Indianapolis, Indiana	184.7
Louisville, Kentucky	183.6
Providence, Rhode Island	153.4
New York City, Borough of Queens	125.5
St. Paul, Minnesota	88.8

The statistics presented show that the mortality from tuberculosis in the Philippine Islands, both in the provinces and in Manila, is greatly in excess of the rates in other countries. I believe that this is absolutely unnecessary and that the climatic conditions of these islands are such that the people should lead an outdoor life and be free from tuberculosis.

There is practically no tuberculosis among cattle and hogs in the Philippine Islands. Of 60,000 hogs and 30,000 cattle slaughtered in Manila during the year 1909, not one was found to have tuberculosis. This surely argues against the climate being the cause of the great prevalence of the disease.

From a somewhat intimate association with the natives throughout a considerable area of the Islands, I believe that we can charge this great mortality to the following causes: Bad hygienic surroundings, poor food, and improper clothing.

The habitation of the native Filipino is badly ventilated, and, in most instances, is very dirty. Especially is there a lack of air during the night, when he adds a smoky lamp, further to pollute the air he breathes. An actual count of 200 houses in Manila, of all classes, made about midnight, showed that less than 25 per cent of them had a window open. The thatched cottages of the poorer natives seem to be well ventilated, but should the visitor have occasion to enter one of those buildings at night, the delusion would soon be dispelled.

The Filipino is a great expectorator and deposits his sputum whenever and wherever most convenient, and it is not uncommon to find the wall and the corners of the room soiled with expectoration.

Ninety per cent of the inhabitants are the hosts of animal intestinal parasites. Investigations conducted in Bilibid have shown that these unwelcome guests greatly increased the mortality among the inmates.

The average native seems to be poorly nourished, his diet consisting largely of rice and fish and a little fruit, with an occasional meal of pork or beef. Much of the fish that is eaten is dried, and a considerable portion of it appears to be decomposed.

Cotton cloth is generally used for clothing and is very inadequate, especially during the rainy season, when shivering natives are a common sight.

The prevention of tuberculosis is receiving the attention of the Bureau of Health, and it is planned to establish a night camp in the vicinity of Manila, and a dispensary for the treatment of cases of tuberculosis is now in operation. The field is large and the resources of the Islands will not allow the sanitary authorities sufficient funds to establish such institutions throughout the Islands. If anything is to be done in combating this disease, the well-to-do inhabitants will have to establish dispensaries and hospitals in the smaller towns. To accomplish this, there should be organized an association, having for its object the prevention of tuberculosis by providing institutions for its treatment and by disseminating the knowledge of the mode of its transmission to the people of the Islands. Were such an association established, it is believed that the philanthropic American citizens who have ever been willing to furnish funds for the establishment of missions in foreign countries would supply money to assist in this campaign.

MALI-MALI, A MIMIC PSYCHOSIS IN THE PHILIPPINE ISLANDS. A PRELIMINARY REPORT.

By W. E. Musgrave and A. G. Sison.

(*From the Department of Clinical Medicine, Philippine Medical School, Manila, P. I.*)

Between *spasm* on the one hand, with its more or less appreciable physical pathology, and the true psychoses, with theoretic or intangible mental pathology, on the other, there exists a neuropsychosis which is interesting and important by reason of its prevalence and confusing because of the illusiveness of its pathology. The habit spasm, habit chorea, *tic convulsif*, of the French, and the other true tics, are found toward the material or physical end of this group. Next comes Gilles de la Tourette's disease, or impulsive tic, with its various manifestations which appear to be real tics modified by a coexistent mimic habit. Finally, the saltatory spasms, at least in part, possibly the myriachit of Siberia, probably latah of Java, and surely mali-mali of the Philippines, are not true tics, but directly and exclusively mimic habits.

The underlying etiologic factor in all these conditions probably is very similar: They are expressions of degeneracy. However, the clinical types are so numerous and vary so greatly that in the absence of a tangible pathology and etiology of these affections, much confusion, particularly in nomenclature, exists and not much order will be possible until the former are more definitely established.

Spasm is defined by Meige and Feindel as "the motor reaction consequent on stimulation of some point in a reflex spinal or bulbo-spinal arc. The irritation provocative of the spasm is itself of pathological origin, and no spasm can occur without it." If this definition is accepted, spasm should be less frequently confounded with tic than often is the case, notwithstanding the close relationship and the rather frequent association of the two conditions in the same individual.

Tics are less definite. Charcot[1] considered tic as a psychic disease in a physical guise, the direct offspring of mental imperfection. Ballet[2] believes that the vast majority of sufferers from tic belong to a class which he designates as "superior degenerates." "The striking feature of these 'superior degenerates' or unstables

[1] Lecons du mardi (1887–88), 124.

[2] Traite de medecine, 6.

is not the insufficiency, but the inequality of their mental development. Their aptitude for art, literature, poetry, less often for science, is sometimes remarkable; they may fill a prominent place in society; many are men of talent, some even of genius; yet what surprises is the embryonic condition of one or other of their faculties. Brilliance of memory or of conversational gifts may be counteracted by absolute lack of judgment; solidity of intellect may be neutralized by the more or less complete absence of moral sense."

Meige and Feindel[3] call particular attention to the practically constant "mental infantilism" as a feature in the character of the patient suffering from tic. Mental infantilism is evidenced by inconsequence of ideas and fickleness of mind, reminiscent of early youth, and unaltered wth the attainment of the years of discretion.

Mere repetition does not, can not, evolve a tic except in patients with psychic predisposition in the shape of volitional enfeeblement. This degeneracy may consist of decrease, absence, arrest or delay, or in overgrowth, increase, exaggeration; and these contrary processes may coexist in the same individual.

Muscular spasm and other requirements of true tic are present in such conditions as Gilles de la Tourette's disease, and to them are added echolalia, echokinesia, echokimemia, and other forms of mimicry. In some of the saltatory spasms, particularly latah, and positively in mali-mali of the Filipinos, the *autospasm* which is the distinguishing feature of true tic is absent and we have in its place only an uncontrollable mimicry, manifesting itself in various ways, but principally as echolalia and echokinesia or echokimemia.

Meige and Feindel,[4] in discussing tics, state that echolalia and echokinesia, in spite of their frequency among those who are addicted to tic, can not be enumerated with the tics, because their exhibition is dependent on the actions of others; whereas once a tic is established it requires no stimulus from without for its manifestation. Of course, their affinity to the tics is very close; they spring from the same soil; they represent in the adult the persistence and amplification of the child's propensity for imitation, and, therefore, in their own way postulate a degree of mental infantilism.

Although these and other forms of mimicry are thus recognized as being independent of auto-stimulation, they are generally classified as tics and, except in the discussions of latah of the Malays by O'Brien, Guinon, Scheube, and others, we have found no literature recognizing the existence of the condition, except as a manifestation in patients suffering from some form of tic.

The "running amok" common among some tribes of the Malays is of particular interest to medical men in the Far East. This disease or one very similar to it is quite common among the Moros of the Philippine Islands, and a number of soldiers and others have fallen victims to fanatical *"juramentados"* [5] during the period of our residence in the southern parts of the Archipelago.

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[3] Tics and Their Treatment (1907).

[4] *Loc. cit.*

Amok is a Malay word and translated means a frenzied desire to murder. It is a neuro-psychosis belonging in the group with Tourette's disease, and should be classified with the tics, at least to the extent that the spasm in both "running amok" and "juramentado" may be autogenetic and may exist entirely independent of any outside influence. The attacks are brought about in two ways. In one it is preceded by days of melancholic stupefaction in which the patient becomes morose, gives up work, and avoids his fellows. In other instances, and particularly in "juramentados," the attacks are brought on by religious rites, incantations, music, dancing, and other methods of psychic stimulation similar to the war dance used by the American Indians. In either case, when a sufficient frenzy is reached, the afflicted person suddenly runs into a crowd of soldiers or other people, or through the streets of a town, and with his *kris*,[6] or among the Moros of the Philippines, with his *barong*,[7] kills whoever may come in his way regardless of age, sex, race, or any other of the usual considerations of affection or fear. One of these patients will charge into a company of armed soldiers with the same recklessness as into a group of defenseless women or children. The fanatic is either killed on the spot, or the attacks last from a few hours to days and usually are terminated by exhaustion or suicide. This disease occurs almost entirely among men.

However, it has a close but much less dangerous and less severe counterpart in a very common and previously undescribed condition among Filipina women, a condition called *dalahira* by the natives and which really consists in a frenzied desire to quarrel. A woman so afflicted will begin to quarrel with a relative, friend, or entire stranger, and will rapidly work herself to a perfect frenzy of speech and gesticulation, without any apparent object. This frenzy may continue for hours, or until terminated by exhaustion, only again to be repeated as opportunity affords. This disease is not the usual expression of anger for cause, but a habit tic or frenzy.

Probably the affection most closely resembling mali-mali of the Philippines is latah.

Indeed, Scheube and some other experienced observers regard the diseases as identical. Scheube [8] considers latah as a form of cerebral neurosis characterized by involuntary movements and incoherently uttered sounds or words. The movements are introduced, accompanied or followed by disconnected sounds or words; the symptoms may arise from fright and may be continued indefinitely as a form of mimicry. All of these patients are easily alarmed, they are for the greater part women of the poorer and more ignorant classes, and heredity seems to play a part in the etiology of the disease.

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[5] *Juramentado.* A term used by the Spaniards and still continued, designating a Mohammedan (Moro) fanatic, who, after certain religious rites, undertakes to kill whom he can until he himself is killed.

[6] A long wavy-edged dagger.

[7] A heavy knife with an approximately straight back and a curved edge. In the Philippines the *kris* is a ceremonial sword.

[8] Diseases of Warm Countries. Jena, 2d ed., (1903), 514.

Scheube [9] believes the malady to have something to do with suggestion in
sons with weak will, and Van Brero [10] considers it to be due to the defective
elopment of will power in the Malay. The latter author defines the disease as
ovoked imitative impulsive myospasm." Scheube thinks that *latah* is identical
h mali-mali of the Filipinos and he further includes as synonyms *bohtschi*
Siam, *yaun* in Burma, *myriachit* in Siberia, and *jumping* in North America.

Tics are quite frequently encountered among the Filipinos, particularly
the upper class, and mali-mali, mimicry, echokinesia, echolalia, echoki-
mia, or other form of mimic habit, without the presence of tic, are
nsidered to be quite prevalent among the lower class of Filipinos,
nost exclusively in the females.

The observations of Charcot and Ballet as to "superior degeneracy" as
origin of tics is borne out here, at least to the extent that cases of
are for the greater part encountered among the higher classes, and
rticularly in suggestive relation to genius. With mali-mali the opposite
ndition is found, the cases all occur among the lower classes of the
mmunity, mostly among women and in the presence of a mentality
iich is so primitive that it may hardly be used for comparative purposes.
While the physician hears of many cases of mali-mali, they are difficult
bring under observation in the hospitals, but the following typical case
s been carefully studied in St. Paul's Hospital and may be reported.

Case I. Mali-mali, echolalia, echokinesia, echokimemia.—Isabel de la Cruz,
nale, Filipina, widow, occupation washerwoman. Stated age 59 years, but
pears much older. Has taken about 30 grams of *vino* daily since she was 18
ars old and smokes a moderate number of cigars. Venereal history is negative.
history of hereditary tendencies has been found. Menstruation has always
en normal and regular and ceased without marked disturbance at the age of
. She was married at a very early age and has given birth to six children,
of whom are living and free from symptoms of mali-mali. There is no history
important previous illness.

Present illness.—The patient states that she was a very nervous child, easily
ightened, and that this condition was aggravated by the pranks of her associates.
hen quite a young girl she was much in contact with an older woman suffering
om mimic habit and our patient believes her condition to have been acquired
om much practice in forcing the older woman to imitate words and actions.
ie mimic habit when once started progressed rapidly, and reached its present
atus of echolalia and echokinesia when the patient was still a young girl.

Present condition.—The patient was admitted to St. Paul's Hospital because
a slight accident and the mimic habit was accidentally discovered after she
id been admitted to the ward. The psychosis is a typical mimic habit, confined
echolalia, or mimicry of words, and echokinesia, or mimicry of movements.
here is no tic or other muscular spasm, no autostimulation or desire to continue
y abnormal sound or movement, except by direct stimulation by sight and
und from some person acting as mentor. What may be called her receptive
age is only obtained by first securing the patient's close attention, which may

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[9] *Loc cit.*

[10] *Allg. Ztschr. f. Psych.* (1895), 2, No. 5.

be done by sudden loud exclamations or quick, spasmodic movements. After attention is thus secured, a remarkably consistent mimicry of words, sounds, and actions may be continued at the will of the operator. The performance resembles that seen in mesmerism, and the face of the patient during these times has the blank, uncertain character of a person under hypnotic influence.

Physical examination of the patient is practically negative. The patellar reflexes are slightly exaggerated, there is no disturbance of sensation; attention, memory, and coördination are good, and there is absolute freedom from muscular spasm of any kind. The mental condition is equal to that of the average poor, ignorant person of her station in life.

In summarizing this case and that of three others, which are not given in detail, it may be stated that they are free from any form of muscular spasm, explosive utterance or other evidence of autospasm or tic. They are characterized by the existence of a temporary abulia, or even by a kind of hypnotic state as it were, under the influence of another person. The presence, amount, and character of the echolalia, or mimicry of words, as well as that of the echokinesis, or mimicry of actions, are entirely under the control of the person influencing the patient.

In order to control one of these patients, unless an extreme degree of susceptibility is present, it is first necessary to secure her attention by a sudden movement, noise, or quick exclamation in a rather loud voice. After this has been accomplished the mimicry may be continued at the will of the operator with no especial effort or concentration.

CONCLUSIONS.

1. The peculiar mimic psychosis in the Philippines known by the local name mali-mali is closely related to, but distinct from, the tics.

2. Such somewhat doubtful tics as Gilles de la Tourette's disease, jumping tic of Beard, myriachit of Hammond, saltatory cramp of Bamberger, latah of O'Brien, tarentism, and the saltatory tics in general, have much in common with the Philippine affection, but in all of these, with the possible exception of latah, there are indications of autospasm which is lacking in the local disease.

3. Ramaneniana, the dancing mania of Ramisiary, St. John's, and St. Guy's dance, and perhaps other allied conditions, are more nearly hysterical manifestations; and while they have much in common with mali-mali they all show evidences of autostimulation, and when once established are capable of prolongation without any outside influence.

4. Mali-mali is probably an expression of mental degeneracy similar to that generally accepted for other conditions of the same group. However, its clinical manifestations do not fully agree with those given for any other similar disease, and for this reason it is classified, tentatively at least, as a *clinical* entity.

DISCUSSION ON THE PAPER, "STATISTICAL STUDIES OF UNCINARIASIS AMONG WHITE MEN IN THE PHILIPPINES," BY DOCTOR CHAMBERLAIN.

Dr. Aldo Castellani, professor of tropical medicine and lecturer on dermatology, Ceylon Medical College, delegate from the government of Ceylon.—I would like to say just a few words in regard to Major Chamberlain's paper, which is a most interesting one. The subject of uncinariasis is one of great practical importance in the Tropics and in subtropical countries. In some districts of Ceylon about 65 to 75 per cent of the people are affected with uncinariasis.

I think Doctor Chamberlain is quite right when he says that even a small number of agchylostomes is of great importance, as secondary bacterial infections may take place through the small lesions produced by them in the intestinal mucosa.

In connection with uncinariasis, I would call attention to a symptom seldom mentioned in text-books: *Fever*. If a temperature chart be kept of all uncinariasis patients, it will be found that in about 20 per cent of the severe cases, fever is present. This fever is generally of a low type, intermittent or remittent, rarely continuous.

Dr. E. R. Stitt, surgeon, United States Navy, associate professor of medical zoölogy, Department of Tropical Medicine, Philippine Medical School, Manila, P. I.—In connection with the question of the period of time a man may remain infected with the hookworm in the absence of the possibility of the removal of the infection, the experience at the United States Naval Medical School with the infection of dogs with *Agchylostoma* is interesting.

In the school there are two classes, one of which, in the practical study of medical zoölogy under Doctor Stiles, performs autopsies on dogs killed at the municipal pound during the autumn months, and the second class do their work in the late spring months. We have observed that the dogs autopsied in the autumn show very heavy infections, while in those autopsied in the spring the hookworms give very small numbers. These observations extended over several years. From this it would seem that the dog became free of his infection during the winter and reinfected himself the following summer. When one considers the formidable teeth of the dog hookworm imbedded in the intestinal mucosa, it would seem that at any rate *Necator americanus,* with only chitinous plates, should be more readily eliminated by man.

DISCUSSION.

. Victor G. Heiser, Director of Health for the Philippine Islands, ssor of hygiene, Philippine Medical School, Manila, P. I.—The r of Major Chamberlain is an excellent résumé, presented in an esting manner, of the work done in connection with the hookworm serves as an example of how wrong deductions may be drawn from nsufficient number of observations. For instance, as a result of the) or more stool examinations which were made of the prisoners at id, over half of the prisoners were found to be infected with worms, and by eliminating these parasites the mortality was reduced 75 to 12 per cent per thousand. There seemed to be no question the reduction in the mortality was due to the elimination of tinal parasites, and more especially the hookworm, because the ment was carried out by brigades, which consisted of 300 prisoners, more than a year was consumed in this work, and the death rate among those prisoners who had been freed of their intestinal sites. At that time many medical men were inclined to reason the same percentage of infection must exist among the general lation, and that if the intestinal parasites could be eliminated a tality rate as low as that found in the Temperate Zones might be ined in the Philippines. However, since it was shown that the entage of infection among the general population was not over 15 that the majority of those examined showed no symptoms, it was ent that no such improvement in the mortality rate could be expected.

r. Gilbert E. Brooke, port health officer, Singapore, delegate from the its Settlements, Singapore.—In Singapore we have not had much rience with this disease. On the quarantine station we do a certain ber of post-mortem examinations of coolies who die at the station, it is very rarely that we find many cases of this infection. During olera epidemic on the station, I found at one time that eucalyptus which we were giving as a cholera prophylactic, resulted in the lsion of numbers of agchylostomes. This oil might therefore prove nirritating and useful vermifuge.

r. J. M. Atkinson, principal medical officer, Hongkong, delegate from government of Hongkong.—I quite agree with Doctor Castellani in king Major Chamberlain for his interesting paper. Was there any record in the old Spanish days of the presence of *Agchylostomum denale* in the Philippines?

ases are seen at the Government Civil Hospital, Hongkong, but disease is not common there and the parasites are generally found n examining the stools of patients admitted suffering from other ases.

f, as I understand Doctor Chamberlain, the white troops from the ted States have in all probability introduced *Necator americanus* these Islands, could not this be prevented by a special medical mination of those men before leaving the States?

Where in the United States is the *Necator* prevalent, and what is the cause of this prevalence? It would be of interest to know the name of the variety found in dogs.

I am afraid my remarks are full of questions. My only excuse is that we delegates are thirsting for information.

Dr. Paul C. Freer, Director, Bureau of Science, dean, Philippine Medical School, Manila, P. I., president of the Far Eastern Association of Tropical Medicine.—Can any one give us the name of the hookworm in dogs?

Dr. Richard P. Strong, Chief, Biological Laboratory, professor of tropical medicine, Philippine Medical School, Manila, P. I.—The species of hookworm found in the dog is the same species, *Agchylostoma trigonocephalum,* which has been described in Europe as giving rise to the pernicious anæmia of hounds.

Dr. Isaac W. Brewer, Medical Reserve Corps, United States Army.—Has the American form been found among the Filipinos?

Dr. W. P. Chamberlain, Major, Medical Corps, United States Army, president of the United States Army Board for the Study of Tropical Diseases as They Occur in the Philippine Islands.—In regard to the last question, all the records that I have seen mention only the American hookworm. I have not seen a report of any other. The American hookworm was first described by Stiles in 1902 and therefore the Spanish records prior to the American occupation would not show its occurrence. Previous to 1902 all human uncinaria were referred to as the *Agchylostomum duodenale.* The occurrence of uncinariasis among American soldiers who had never been out of the United States was entirely overlooked until Siler's work in December, 1908. Therefore, the physical examination given in the past to soldiers about to start for tropical service had not included a search for intestinal parasites. At the present time it is the practice at some and perhaps at all recruiting stations to examine the stools of recruits at the time of enlistment and treat all whose stools show ova. Practically all of the infected soldiers I have seen were so mildly infected that the condition would be entirely unsuspected on ordinary physical examination. That the *Necator americanus if present among whites,* may cause very marked and serious symptoms has been shown by investigations in the Southern States and among natives in Porto Rico. *Necator americanus* has been found commonly among the Filipinos.

I suppose, Doctor Castellani, this hookworm is found in Ceylon?

Doctor Castellani.—We have both species.

Doctor Chamberlain.—Has anyone seen *Agchylostomum duodenale* of late years in the Philippines?

Doctor Strong.—Both species, *Uncinaria duodenale* and *Necator americanus,* are found here. Doctor Garrison has recently identified specimens which are deposited in the museum of the Biological laboratory. I first reported the presence of *Agchylostomum duodenale* in the Islands in 1900. At that time the species *Necator americanus* was not known, but the anatomic description given of the parasite encountered here shows that the species then described was not *Necator americanus.*

DISCUSSION ON THE PAPER, "MYZOMYIA ROSSII AS A MALARIA-CARRIER," BY DOCTOR VOGEL.

Doctor Strong.—I am very much interested in the results of Doctor Vogel's experiments. About two years ago Mr. Banks, of the biological laboratory, reported that *Myzomyia ludlowii* was capable of transmitting malaria in the Philippines. We now know that this species is identical with *Myzomyia rossii.* During the past year in connection with the work in the courses of tropical medicine in the Philippine Medical School relating to the study of malaria, we attempted to infect numerous specimens of *Myzomyia rossii* by exposing patients suffering with severe cases of æstivo-autumnal and tertian malaria to their bites. However, although these experiments were extensive and were carried on over a period of several months during the autumn, they were entirely unsuccessful. In no case did the dissection of any of these mosquitoes, although a large number were examined, reveal any oöcysts in the walls of the stomach, and in the study of stained sections made of the salivary glands no sporozoiites could be detected. Later attempts to infect other human beings by the bites of specimens of *Myzomyia rossii* which had been previously fed on the blood of patients suffering with severe malaria and whose blood certainly contained gametes, also failed. The larvæ of these mosquitoes were collected in the estuaries about the city.

In connection with Doctor Vogel's experiments the results we obtained are interesting. We know that these estuaries are affected by the tides and that more salt water would naturally enter them when the tides are high and that after the season of the high tides has passed, more salt would therefore be deposited in the marshes. In this way the breeding places of these mosquitoes would at times contain a greater amount of salt than at others.

I do not recall at what time of the year Mr. Banks' experiments were made. It would certainly be important to ascertain what effect, if any, these changes in the character of the breeding places would have on the transmission of malaria by *Myzomyia rossii.*

Mr. Charles S. Banks, Biological laboratory, Bureau of Science, lecturer on medical entomology, Department of Tropical Medicine, Philippine Medical School, Manila, P. I.—The paper by Doctor Vogel is certainly a very interesting one in that he has emphasized practically the same conditions that I found at Olongapo, in my work upon the transmission of malaria by *Myzomyia rossii*.[1] I might also say that in the Province of Lepanto-Bontoc, where the town of Cervantes is situated, many miles from any possibility of salt-water influence, I found this mosquito breeding in sluggish streams of purely fresh water. The parasite was found in great abundance in the blood of the natives at this latter place. I may state, in referring to the question of the saltness of the water, that I did my first work at Olongapo, where I bred this mosquito. Topographically, Olongapo is like Manila, except that the ramifications of the land are not so extensive and all the estuaries in the vicinity are affected by the water of Subig Bay, which is as salty as that of Manila Bay and the China Sea.

I doubt very much if the mosquito in Manila could be said to breed in water which is not salt. As far as I have found, this mosquito is prevalent only in the estuaries of Manila that are distinctly affected by rising tides.

DISCUSSION ON THE PAPER "ANTIMALARIAL PROPHYLACTIC MEASURES AND THEIR RESULTS AT THE NAVAL STATION, OLONGAPO, P. I.," BY DOCTOR DUNBAR.

Mr. Banks.—The observations of Doctor Dunbar are identical with my own at Olongapo. It was certainly true that the largest percentage of Marines who had malaria had been sent to the navy rifle range for target practice and were therefore in a region abounding in malaria. As Doctor Dunbar says, there was a great increase in malarial infection as the dry season advanced.

I have a map, which anyone may see who wishes to, which shows the topography of Olongapo and also the location of the mosquitoes as I found them. The point regarding the inadequacy of mosquito nets was also brought out by me in my paper. The different seasons of the year strongly influence the abundance of the mosquitoes. It is a well-known fact that they can not exist during the rainy season. The hard rains destroy them, as the larvæ remain on the surface of the water. During the dry season there is no such menace to their existence.

Doctor Highet.—I should like to refer to two interesting measures on antimalarial work which were carried out in Siam, one of which was of special interest.

The first experiment was performed on the old quarantine station of Bangkok, situated on the Island of Koh Phai, in the Gulf of Siam, and some few miles from the mainland. There *Anopheles* mosquitoes abounded and malaria was of a very severe type, but after carrying out the usual work in accordance with the instructions of Ross, mosquitoes disappeared and along with the malaria. Quinine, which formerly was employed by ounces per week, was no longer necessary. This is a typical case of success following upon the destruction of the breeding grounds of the *Anopheles*.

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[1] *This Journal, Sec. B* (1908), 3, 335.

Being compelled to change the site of the quarantine station, another island was chosen, Koh Pha. Upon landing upon this island for the purpose of determining the suitability of it for a quarantine station, a small marsh was found teeming with *Anopheles* of a very virulent nature. Nevertheless, this island was fixed upon for the location of the station, buildings were erected for the staff and coolies, and, although fever was common at first even under the influences of prophylactic doses of quinine, the results of antimalarial methods soon became evident. However, while the police and the general staff of servants, etc., began to show freedom from malaria, the medical officer, his wife and family continued to suffer severely from fever. Being certain that there was a flaw somewhere, I visited the station, and after a careful inspection of the whole station discovered a water jar at one corner of the medical officer's house, half full of water and teeming with *Anopheles* larvæ. These were destroyed and now that medical officer's successor and his wife and children enjoy excellent health.

Dr. Henry Page, major, Medical Corps, United States Army, Manila, P. I.—I understand from the Spanish records that the post of Parang in Mindanao was considered one of the most deadly in the Philippine Islands. At the present time there is practically no malaria there and very few mosquitoes. After the post itself was almost entirely free from malaria, a marsh was found near the last barracks which appeared to have an influence upon malaria, so we finally had it drained. The result was, the soldiers testified that whereas before they never were able to sleep at all because of the mosquitoes, they now never see a mosquito.

At another part of the post where the people were complaining of the mosquitoes, I had banana trees and ornamental shrubs cut away and thus rid the fort of mosquitoes. The point emphasized is that a marsh several hundred yards from the post supplied a bountiful crop of mosquitoes, even though the prevailing winds blew from the post toward the marsh; and, second, that banana plants can breed mosquitoes in a country where frequent, gentle showers and heavy dews fill up the cup between the stalk and its junction with the leaf.

Just a word as to prophylaxis in the field in regard to the protection of the men from mosquito bites when asleep under their nets when the arms and feet usually were thrown against the net offering opportunities of exposure to the insect, I requested soldiers to put their beds together in pairs with the sides of their individual nets tied close together. By doing this, they were able to escape from the unprotected sides of their nets to the protected side, and I observed that when such an arrangement was made few men suffered from the insects. Of course, it is very objectionable for people to sleep together, for many reasons, but in cases like this it seems advisable.

Major Hooton, I. M. S., Rajkot, Kathiawar, India, delegate from the government of India.—I have listened with great interest to Doctor Dunbar's paper and think that, especially at the present time, when it appears to be the opinion of some authorities that prophylaxis by mosquito destruction, on the lines recommended by Ross, is for the most part impracticable on the score of expense and for other reasons, it is most important that instances in which it has been successful should be put on record. Personally, my own experience entirely corresponds with that of the previous speakers. I have lived in several Indian stations where a notable decrease of mosquitoes has followed the usual measures of destruction, and have recorded, in one instance, an almost total disappearance of malaria and I think it is obvious that under the conditions prevailing in many Indian towns and villages action on these lines, properly carried out, must meet with success. There are, of course, certain localities where quinine is the only possible means of prophylaxis, but I would urge that these are exceptional and that quinine should be regarded on the whole as of secondary importance to the destruction of mosquitoes. Another point is that the abolition of collections of waste water goes hand in hand with general sanitary measures.

I think it would be an excellent thing if the opinion of this meeting could be taken as to the general practicability or otherwise of Professor Ross' measures.

Doctor Atkinson.—Our experience in Hongkong, during the past ten years, have proved entirely confirmatory of the beneficial results arising from applying Professor Ross's method of mosquito destruction in a malarial district. I have instanced the case of MacDonald Road in Hongkong. Malaria was very prevalent there in 1900 and 1901. In the winter of 1901 and 1902, active antimalarial measures were carried out, viz, removal of brushwood and undergrowth around the house, training of the nullahs and drainage of all collections of standing water. In addition, an active fumigation with sulphur of the coolie quarters attached to the houses was carried on. The result is that now in the district where previously malarial fever was very prevalent, *no* cases occur.

Doctor Brooke.—While most of us seem agreed on the admirable results which can be obtained by mosquito destruction, quinine prophylaxis, and general sanitary measures, no speaker has yet mentioned the valuable aid to antimalarial campaigns which can be rendered by legal enactments.

Ordinances have recently been passed in the British East Indies making it a legal offense on the part of a householder or occupier to have any living mosquito larvæ in any vessel or collection of water within his household or compound.

In large, native, tropical towns this might offer some difficulties, but in a town with such excellent sanitary methods and administration as yesterday we had demonstrated to us in Manila, the addition of a "larva column" to the householder's sanitary sheet might be a feasible matter.

Doctor Francis Clark, medical officer of health, delegate from the Government of Hongkong.—Doctor Dunbar has told us that by clearing and filling within a radius of 200 feet around the buildings at Olongapo malaria disappeared, but I am of the opinion that this will only be for a time. In Hongkong we have, as you know, to deal with mountain streams, and it is no easy matter to train these streams by confining the water to one smooth channel throughout so as to prevent the development of mosquito larvæ. Just to show you what occurred in one district: In the western section of the city are many European houses, and near these houses are several streams. The nearest stream was examined for *Anopheles* larvæ and many found in it. This stream was within about 30 to 50 yards of the nearest houses. The next stream, further west, was at this time found to contain no *Anopheles* larvæ; and so with the others, still further west. The first stream was trained and confined to a smooth channel in which mosquito eggs and larvæ could find no lodgment. The result of this work was that malaria disappeared from this district. This condition lasted two or three years and then malaria again broke out. I went, together with Doctor Thompson, our mosquito expert, and thoroughly examined all these streams, both trained and untrained. The trained streams were clear of larvæ, there being no possibility of their lodging there, owing to the fact that these trained streams are all carefully watched, defects remedied and the channel scrubbed once a week with hard brushes to prevent the growth of algæ at their margins, as we have found that the latter will serve for the development of mosquito eggs.

In the first untrained stream, however, *Anopheles* larvæ had now appeared. This seems to indicate that *Anopheles* like the neighborhood of houses, and when they are driven out from the immediate neighborhood of a dwelling they will, in the course of two or three years, appear in the nearest stream and many find their way thence to the houses, if the latter are within flying distance. What the limit will be I can not tell, but we hope 400 yards will be sufficient. We must push our efforts certainly a quarter of a mile from the nearest dwellings, and even then it is necessary to watch the nearest water courses for the reappearance of *Anopheles* larvæ.

Mr. Banks.—I would like to say that we can not give too much attention to the habits of the different species of mosquitoes. I have always found *Myzomyia rossii* Giles and other *Anophelinæ* breeding in running water which had some current in it and in which green algæ were to be found growing in the surface, as you will see in the specimens downstairs in the exhibit. Mosquitoes have habits as distinct as domestic and wild animals, such as the dog, the cat, the lion, the bear; and the only way intelligently to combat them is by first obtaining an intimate knowledge of their habits.

Doctor Castellani.—Malaria prophylaxis based on mosquito destruction is of the greatest importance, and I am very much in favor of it, but at the same time we should not forget how useful quinine prohylaxis also is. I would call attention to the splendid work of Professor Celli in Italy. He has succeeded in having passed through both houses of Parliament laws by which quinine is manufactured by the State and supplied *gratis* to the poor people in the malarial districts of Italy. These legislative measures have been taken up by Greece and Roumania and the results have been most satisfactory.

DISCUSSION ON THE PAPER "INCIDENCE AND COMPLICATION OF MALARIA IN THE PHILIPPINE ISLANDS," BY DOCTOR BOWMAN.

Doctor Castellani.—Doctor Bowman's paper has been very interesting to me. In Ceylon I have come across many cases of sequelæ and complications of malaria, and I agree with Doctor Bowman that a neuritis, sometimes a polyneuritis, may be of malarial origin.

I have not had much experience in regard to the treatment of malaria with atoxyl. I treated three cases with it, but the results were far from being encouraging. I gave about one-half gram every two days. In one case I had to discontinue the treatment because the patient developed symptoms of arsenical poisoning. As regards arsenophenylglycin, I have not had any experience, but this drug has been shown by Doctor Bowman to have no effect in malaria, and may produce symptoms of arsenical poisoning.

Referring to the treatment of filariasis, I have made some experiments with atoxyl and other drugs and in my experience all of them are useless. However, it has seemed to me that in some cases of chyluria there is a slight benefit from the administration of methylene blue.

DISCUSSION ON THE PAPER "NOTES ON CONTAGIOUS OPHTHALMIA," BY DOCTOR BROOKE.

Doctor Chamberlain.—I am much interested in the subject of Koch-Weeks conjunctivitis because the Army Board for the Study of Tropical Diseases, of which I am a member, has been investigating for two months an extensive epidemic of conjunctivitis among Filipinos on Carabao and Corregidor Islands at the entrance to Manila Bay. There are about 4,000 native laborers employed there in building emplacements for artillery, and during the last year and a half about 1,000 cases of conjunctivitis have occurred. As many of these men have been sent away incapacitated, it is probable that they are spreading infection in their native towns.

We have seen 25 cases of this disease, all presenting severe generalized injection of the bulbar and palpebral conjunctiva. In several cases there were ulcers of the corneal periphery, and in one a large ulcer on the inner surface of one upper lid. The discharge was mucopurulent and never of great amount. Smears were taken in 12 cases and in each one the Koch-Weeks bacillus was demonstrated, sometimes in large numbers. Cultures made on human (Filipino) serum agar gave in four cases a mixed growth of staphylococci and bacilli conforming in size and shape to the Koch-Weeks bacillus. We were not able to obtain a pure culture. Other observers in the Islands have at times demonstrated the Koch-Weeks bacillus in smears from the eye, and it is probably a common and important cause of conjunctivitis here. Major Rutherford, who treated several cases of this disease at the Division Hospital, found argyrol promptly effectual. Isolation is very important, as the disease is extremely infectious, the spread probably being mainly by direct contact and by infected droplets expelled from the mouth and nose.

Doctor Atkinson.—I was very much interested in Doctor Brooke's paper, especially as the presence of trachoma occurring among Chinese emigrants leaving Hongkong has been a very vexed question. I refer especially to those proceeding to the ports of the United States. I was glad to hear the confirmatory conclusions of Doctor Brooke, that trachoma is a distinctly rare disease among the Chinese emigrants at Singapore.

The presence of a *Gram-positive organism* in many of the cases, distinct from the Koch-weeks bacillus, is also worthy of note. I would like to ask Doctor Brooke whether this is easily seen in a smear of the conjunctival discharge, in other words, the technique of finding it.

Doctor Strong.—I would like to ask Doctor Brooke and any others present who have studied epidemics of conjunctivitis in tropical countries from a bacteriologic standpoint, as to whether they have encountered the *Bacillus xerosis* in any of their cases? In 1900 I studied in the First Reserve Hospital in Manila a number of cases of conjuctivitis from which *Bacillus xerosis* was isolated. This organism is easily cultivated. Inoculation of animals with the Gram-positive organism described by Doctor Brooke might aid in elucidating the nature of the organism.

Doctor Castellani.—I think Doctor Brooke should be congratulated on his interesting address. Sir Allan Perry and myself, in the last four years in Ceylon, have investigated a large number of cases of conjunctivitis among the natives and Europeans. In some cases we observed the Koch-Weeks bacillus, which we found most difficult to cultivate. In some other instances we encountered the diplobacillus of Morax, and in about 15 or 20 per cent and in a certain number of normal people we found a Gram-positive, nonmotile organism which we considered identical with the *Xerosis* bacillus.

Dr. Henry Fraser, director, Institute for Medical Research, Kuala Lumpur, delegate from the government of the Federated Malay States.—Some five years ago I took part in an extensive investigation on the bacteriology of conjunctivitis. We devoted the first year to learning methods and thereafter made a bacteriological and clinical examination of every case of conjunctivitis admitted during one year to the ophthalmic department of the hospital and the public dispensary. Nearly 1,000 cases were dealt with in this way.

Conjunctivitis caused by the Koch-Weeks bacillus is an acute infection. A lotion of boric acid to remove the discharge and keep the eyes clean is all that is necessary.

Conjunctivitis caused by the diplobacillus most frequently runs a chronic course. It can readily be cured by the instillation of drops containing zinc sulphate. These drops sting when they come in contact with the conjunctiva, so that the treatment in the hands of laymen may prove ineffective, but when properly applied a cure must result. The use of silver salts in either of these forms of conjunctivitis is unnecessary.

The cultivation of the Koch-Weeks bacillus is easy on ovarian agar. The bacillus staining by Gram and described by Doctor Brooke is in all probability the *Bacillus xerosis.* This organism is frequently found in cases of conjunctivitis, as has already been stated.

Dr. Allan J. McLaughlin, passed assistant surgeon, United States Public Health and Marine-Hospital Service, Assistant Director of Health, assistant professor of hygiene, Philippine Medical School, Manila, P. I.—I regret very much not hearing the first part of this interesting paper. I wish to state that I have never yet seen a case of conjunctivitis which did not clear up in a very few days regardless of what bacillus was present. I agree with Doctor Brooke that the first stage of trachoma is indistinguishable from acute conjunctivitis of other kinds. In the rejection at Naples of 15,000 Italian immigrants embarking for the United States, this fact was considered and all having acute conjunctivitis were held. Many cases could then be passed after ten days as not having trachoma. In fact, ten days' treatment usually cleared up a case of simple, acute conjunctivitis, while real trachoma persists after the treatment and goes on to new tissue formation, ulceration and cicatrization. There is absolutely no relation between the conjunctivitis which clears up and trachoma. The two must not be confused. Trachoma is always chronic and is never cured in the acute stage.

Doctor Brooke.—Doctor Atkinson asked a question in regard to the technique. This is relatively easy, even a wooden match will do quite as well as a platinum loop. Get a small flake of mucus from the conjunctival sac and prepare the slide with this, when any organisms present may be seen.

With regard to the possibility of the Gram-positive organism being identical with the *Bacillus xerosis*, I was led to think that they were separated entities from the fact that even in old cultures there were no involution forms of a *diphtheroid* shape. I had always considered *Bacillus xerosis* as not being in any way pathogenic, but merely adventitious as in the case of spirochaetae. The bacillus in any sense seemed sufficiently constant to be causal, but the possibility of identity with *Bacillus xerosis* might certainly be considered, as *Bacillus xerosis* is polymorphic.

With regard to acute conjunctivitis clearing up in a few days and trachoma being an acute disease, I attempted to bring this fact out in my paper.

In referring to the question as to whether acute catarrhal conjunctivitis can be differentiated from the preliminary conjunctivitis of trachoma, by its amenability to treatment, I will state that the point I wished to emphasize was that the condition is the earliest symptom of trachoma and in mild cases the connection between the two might be overlooked, with grave results.

DISCUSSION ON SIR ALLAN PERRY'S PAPER, "THE PRESENT POSITION OF THE LEPER IN VIEW OF THE RESOLUTIONS PASSED AT THE INTERNATIONAL CONFERENCE ON LEPROSY AT BERGEN, 1909."

Major Hooton.—It seems to me rather early to condemn Professor Deycke's treatment. Not long ago I had an opportunity of seeing a number of lepers at the Matunga Asylum in Bombay who had been injected with nastin for various periods, and there were among them many cases of the nodular form of the disease which, to judge from photographs previously taken, and from the statements of the patients themselves, had improved very markedly as regards both the local and general conditions.

Doctor Atkinson.—This disease is rife in the Philippine Islands, in China and elsewhere in the Orient. Plague is also rife, and since this is the first time delegates have met in this way, in order that some practical conclusions may be arrived at by this congress, I move that subcommittees be appointed to consider and report to the association before the 15th instant what measures they recommend in connection with the following: Leprosy, plague, and quarantine regulations regarding infections diseases. We have here delegates from practically all countries east of Suez, from India, Ceylon, the Straits Settlements, Netherlands-India, Siam, Hongkong, China, and Japan, and we have a grand opportunity for formulating conclusions. If we put off this question until the business meeting which comes the last day of the session, it simply means that no practical results can be reached until the next meeting of the association in 1912.

Doctor Heiser.—I would like to ask Doctor Atkinson to add the opium question to the list he has given. The most excellent paper of Sir Allan Perry again brings to our attention in a most forcible manner the value of the resolutions of the last International Conference on Leprosy at Bergen, because they aid us as health officers in our contention that in order successfully to combat this evil it is necessary to segregate lepers. The Legislature of the Philippine Islands, several years ago, did put into force the principles involved in the resolutions of the international conference, and as has been mentioned by Doctor Perry, the result thereof in the Philippine Islands has been most gratifying, the total number of lepers having been reduced from 4,000 to 2,300, which reduction is believed to be due to the fact that new infections are prevented.

In view of the great prevalence of the disease in oriental countries, and since the delegates to this association represent nearly all the governments concerned, it seems to be most appropriate and fitting that a set of similar resolutions should be favorably acted upon by this Association.

The following committees were appointed by the chair:

Plague.—Doctor Atkinson, chairman; Doctors Highet, Hooton, Castellani and Strong.

Leprosy.—Doctor de Haan, chairman; Doctors Staby, Neeb, Shibayama and Heiser.

Opium.—Doctor Fraser, chairman; Doctors Beebe, Staby, Neeb and Musgrave.

Quarantine.—Doctor Brooke, chairman; Doctors Highet, Atkinson, de Haan and Heiser.

Tuberculosis (local committee).—Doctor Musgrave, chairman; Doctors McLaughlin, Christensen, Andrews and Sison.

Beriberi.—Doctor Highet, chairman; Doctors Strong, de Haan, Fraser and Aron.

The following resolutions were finally adopted by the association:

TUBERCULOSIS.

Resolved, That the Far Eastern Association of Tropical Medicine should use its influence to cause the formation of a national antituberculosis society in each political entity represented in the Far Eastern Association of Tropical Medicine. These societies to be formed along the lines of existing antituberculosis societies in other parts of the words, yet revised to facilitate the work under local conditions.

LEPROSY.

Resolved, That—

1. Leprosy is to be regarded as a dangerous communicable disease.
2. Compulsory notification of all cases of leprosy to the authorities is essential.
3. Compulsory segregation of all cases of leprosy is necessary, and preferably in special colonies constructed for the purpose.
4. The entrance of aliens afflicted with leprosy into a country must be prohibited.

QUARANTINE.

Resolved, That the Far Eastern Association of Tropical Medicine, appreciating the benefit which would accrue from concerted sanitary action on the part of Eastern governments, be empowered officially to approach the following Governments, namely: Philippine Islands, Japan, Hongkong, French, Indo-China, Siam, Netherlands-India, Straits Settlements, and Ceylon, with the view, if possible, of obtaining their official support on the following lines:

1. To have a common standard for the term "epidemic," when making reports to, or imposing quarantine against, each other.

We suggest the following definition for consideration:

Plague, cholera, smallpox, or yellow fever shall be considered to be epidemic, when, after the first telegraphic report of its occurrence, any weekly report thereafter shall show the occurrence of an average daily number of three cases.

2. To agree to notify each other's territories as infected, only when the infectious disease shall have assumed epidemic proportions as defined above; and automatically to withdraw such notification when the average number of cases for three successive weeks has fallen below the status epidemicus as above defined.

3. To circulate weekly returns of plague, cholera, smallpox, or yellow fever amongst each other, and also a telegraphic report on the first occurrence of any of these diseases, in a clean port or territory.

4. To insist on a bill of health being carried by all ships, leaving a country declared to be infected, which intend to proceed to the port of another signatory; such bills of health to include a return of infectious disease for the previous forty-eight hours.

5. To report by telegram to the country concerned the departure of an infected or suspected ship (as defined by the Paris convention) which may intend to proceed to any port in the territories of another signatory; and to indorse the bill of health of the said infected or suspected ship with a full account of measures taken to disinfect or otherwise deal with the said vessel.

PLAGUE.

Report.—In our opinion the only practical measure concerning plague that we can recommend is the advisability of each country represented agreeing to notify other countries the occurrence of cases of plague within their borders, the first case by telegram and afterwards by weekly returns.

OPIUM.

Report.—Your committee, appointed to consider the *opium* question, regret that the time at their disposal precludes the possibility of giving the subject adequate consideration.

They have reviewed the work done and the resolutions agreed on by the International Opium Commission, Shanghai, 1909.

With these resolutions your committee are in agreement, but it is to be regretted that the paucity of medical commissioners prevented the question being dealt with fully in its medical aspects.

Any measures which are introduced for the control of opium must be adequate to guard against the danger of secret remedies containing opium and opium derivatives being substituted.

They would suggest that the delegates from the various countries represented at this conference should be asked to arrange that the regulations controlling the sale and use of opium in their respective countries, as well as any observations they may care to make on this subject, be submitted to the next meeting of this association in 1912.

BERIBERI.

Resolved, That in the opinion of this association sufficient evidence has now been produced in support of the view that beriberi is associated with the continuous consumption of white (polished) rice, as the staple article of diet, and the association accordingly desires to bring this matter to the notice of the various Governments concerned.

REVIEWS.

L'Insect et L'Infection, Histoire Naturelle et Médicale des Arthropodes Pathogènes. Par Raphaël Blanchard, Professeur à la Faculté de Médicine de Paris, membre de l'Académie de Médicine. 1er Fascicule: Acariens, 8°, 167 pages avec 197 figures dans le texte. Prix, broché 6 francs (=$1.20) Paris, Libraire Scientifique et Litteraire, 4, rue Antoine-Dubois, Mai 1909.

The first fascicle of this very important work has recently come to our hand. As the distinguished author says: "The work is intended to set forth the important and very little known rôle played by the three groups of Arthropods in the propagation of infectious diseases: Arachnida, Myriapods and Insects, all classed under the general term Insect."

This portion of Doctor Blanchard's work deals solely with the *Acarina*, including the ticks and mites. The first chapter considers definitions of the *Acarina* in general and the family *Ixodidae* or ticks; the second deals with their morphology and anatomy; the third with their evolution and biology; the fourth with their systematic study and descriptions of genera and species. In these chapters nothing seems to have been omitted which will serve the average medical man in becoming acquainted with the group, both from the zoölogical and medical standpoints. The descriptions of organs and the account of the life history of ticks are treated in a manner at once clear and comprehensive, while the tables and descriptions of genera and species make the classification of the ticks which will usually be met by the physician and veterinarian comparatively easy.

The systematic works on this group by Nathan Banks, the American authority, have been freely requisitioned as have those of Dönitz, Pocock, and Salmon & Stiles. This, together with Doctor Blanchard's profound knowledge of the group has made his work the most up-to-date and complete of anything that has recently appeared.

The illustrations, of which there are some 197 in the text, are all carefully prepared and lucid. The bibliography is not what the word implies, as it simply indicates the authors who have worked on the groups and the date of their publications without the titles. However, it may be that Doctor Blanchard intends to append a bibliography to the last part. The work is to be completed in three or four parts and the remaining numbers are to deal with the *Diptera* (flies, including mosquitoes), the *Aphaniptera* (fleas) and the *Hemiptera* (bedbugs, lice, etc.).

A work of this character is certainly invaluable to the physician, especially in isolated tropical regions where access to libraries is not possible and where he needs to have a comprehensive digest of *all* that relates to insects and infection.

CHARLES S. BANKS.

Mammalian Anatomy With Special Reference to the Cat. By Alvin Davison. Second edition. Pp. 246. Price $1.50 net. Philadelphia: P. Blakiston's Son & Co., 1900.

As the author states in the preface to the second edition, it is only a few years since medical schools have expected their students to enter with some knowledge of mammalian or comparative anatomy. It is now only a matter of time until all medical schools will require either a good course in comparative zoölogy, or in mammalian anatomy (perhaps both) as a prerequisite to entrance.

There is also a strong and growing feeling in the United States that college graduates in general should have an understanding of human anatomy and physiology. Davison's book is merely the last of several which have been prepared in response to these demands for the study of mammalian anatomy, using either the dog, cat, rat or rabbit as the type. For several practical reasons the choice is limited to the dog or the cat.

The anatomy of the cat is treated in a much better way by Reighard and Jennings, but there are many schools in which so extensive a course can not be given. It is to these that Davison's Mammalian Anatomy is directed. However, the book is too elementary. No student who is preparing for medicine, and probably no other college student, is ready to study mammalian anatomy until after completing a thorough course in zoölogy, which will give him a more or less philosophic conception of the animal kingdom. Without such a course the mammalian anatomy will fail in a large degree to accomplish its purpose. The reviewer believes it to be a mistake, if not an impossibility, to attempt to adapt a text to both elementary and advanced students, as the author has done.

The introductory chapter contains some very useful directions for teachers (certainly they can not be intended for students) regarding the preparation of the specimens for study. Those for the demonstration of the lymph vessels, for the preparation of the central nervous system, and for the cleaning of the bones, are especially good. However, in this day and age, it does seem as if even the most poorly prepared teacher must know what specimen jars and injecting syringes are like; therefore, figures of such objects (figs. 1 and 2) are decidedly out of place in any text-book.

The remainder of the book covers briefly the anatomy of the cat, taking up the parts in the following order: Skeleton, joints, muscles, organs of digestion, vascular system, respiratory system, excretory and reproductive system, and nervous system. The descriptions are usually sufficient. A list of practical questions and suggestions is found at the end of each chapter. The latter are nearly all directions as to the drawings to be made, while the former are intended to direct the student's attention to important characters. It is a fair question if college students should not be expected to learn to see for themselves without such explicit hints. If they do not learn to use close observation, what becomes of the scientist's claim for the educational value of his subject?

The author makes a few observations in every chapter on the comparative anatomy of the Mammalia, but they are so feeble as to have no value, and are of a class generally which should be included in the lectures of the teacher giving the course. The same may be said of the remarks on microscopic anatomy and physiology, which also are found occasionally.

The list of definitions of terms used in osteology is good. The description of the skull is taken up in a new order, but accomplishes its purpose as well as any. The illustrations of the skeleton are the best in the book.

Some of the figures, as 12, 14, 35, 44, 52, and 64, are inexcusably poor. Fig. 88, which is a diagram of the structure of the kidney, is another illustration of the fact that an original drawing is not always an improvement on those already published and available. A figure of a generalized type of carpus (see fig. 36 B) is much better copied from an authority on the subject, and accredited to him, than offered as an original contribution by an author whose study of comparative anatomy has not been extensive.

For the study of the muscles the author gives first a well-drawn figure of each part, and then a table telling the name, origin, insertion, and function of each muscle. The combination is rather too much for the good of the student, and must tend to reduce this part of the course to pure memory work. The figures alone, with a few directions as to procedure, would be sufficient and would compel the student to do real dissection.

The consistent use of the terms craniad, caudad, etc., is not always pleasing. When two organs lie in the head, and one is described as "craniad to" the other, we know, of course, what is meant, but can not help feeling that the use is rather absurd, while the occasional employment of an Anglo-Saxon word would neither be absurd nor incorrect.

The chapter on the organs of digestion is decidedly unsatisfactory. This is the result very largely of the manner in which the author writes his description. As a matter of fact, the reader can not help feeling that every portion of the book proves that the author does not appreciate the power of the English language to express ideas, when properly used.

The discussion of the fiber tracts of the central nervous system belongs to the provinces of special anatomy and physiology rather than to elementary mammalian anatomy. The table of cranial nerves on page 205 will prove convenient and helpful. It seems a mistake not to insist more strongly on a careful dissection of the cranial nerves, especially the vagus; there is nothing definite in the book concerning the course of this nerve and that of the phrenic. The figure of the sympathetic nervous system (p. 107) and the description in the text of the middle cervical ganglion do not agree. The remarks regarding the convolutions of the brain in mammals are misleading, as usual.

A complete glossary is a valuable feature of the book. The text will undoubtedly find a wide use in American colleges, in spite of its failings, for it fulfills the essential requirements of the teachers in those schools.

The work of the publishers has been performed excellently.

LAWRENCE E. GRIFFIN.

A Compend of Histology. By Henry Erdman Radasch. Pp. 350. Price $1.00 net. Philadelphia: P. Blakiston's Son & Co., 1909.

Quiz-compends, which originally were prepared as a first aid to lazy or imbecile students of medicine, are developing for the better along with the improvement of medical education. This little book of Doctor Radasch, though published as one of Blakiston's series of quiz-compends, will scarcely be recognized as belonging to the group of educational pacifiers usually known by that name. It might better be called an outline of histology, since it differs from textbooks of the usual type mostly by the brevity of the descriptions.

In the first chapter (30 pages) the author describes the ordinary processes of preparation of histological material and gives the formulae of the reagents most used. A very limited amount of technique should be expected of students in the ordinary course in histology, while the more complicated processes should not be attempted by the student. Nevertheless, the description of these processes may be a considerable aid by enabling the student to understand the treatment of the sections he is required to study. If this chapter is intended to fulfill such a purpose, its presence may be justified.

This book includes chapters on the fetal membranes, the "nerve system," "the eyeball and lacrimal system," the ear, the senses of smell, taste, and touch, and on the development of the face and teeth. The illustrations are sufficient for a book of greater pretensions.

The author is fortunate in his ability to write short and unusually clear descriptions, which are complete but not tedious. A few of his definitions are open to criticism, for instance when he writes that "metabolism is the *change* that takes place in a cell during the performance of its functions." Possibly the critic is captious, but metabolism seems to be better described as a process than change. Nor is the classification of secretion and excretion as simple as the author states.

It would be very much better if the writers of text-books on histology would not treat of amitosis as if it were an ordinary and common method of nuclear division. To be able to state that cell-division is of two varieties, direct and indirect, seems beautifully clear and simple and appeals to our love of antithesis. As a matter of fact, the probabilities are that the student of histology will never see an example of amitosis, and the chances are that the instructor himself has seen very few cells actually undergoing amitotic division. The student would get a very much more correct idea of its *unimportance,* if amitosis were only described in connection with the tissues where it occurs, and if he were told that amitosis is usually found in decadent or degenerating tissues, and that there exist grave doubts of its being in any sense a normal process in metazoan tissues.

The author should have made it clear that the process of segmentation described on page 42 is not the usual one observed in the animal kingdom, but a very peculiar process limited to some of the mammals.

The mechanical work of the book is done in a very satisfactory manner. Some of the figures and diagrams are original and a few are improvements on the ones usually published. On the other hand, some of the figures copied from other text-books have suffered in the process.

The principal criticism of the book is that it offers nothing which other texts do not give in a better way. It escapes being a real quiz-compend, but does not attain the dignity of a text-book, while it is certainly not a laboratory manual. For the teacher who wishes to give as extensive a course in histology as is outlined in this work, there exist several text-books which are so much superior to it in the treatment of the subject, that Doctor Radasch's book can not be compared with them.

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THE PHILIPPINE

JOURNAL OF SCIENCE

B. MEDICAL SCIENCES

VOL. V OCTOBER, 1910 NO. 4

TOLERANCE FOR ALKALIES IN ASIATIC CHOLERA.[1]

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The symptoms of Asiatic cholera, in comparison with those of other acute bacterial infections, present some unusual features. Although the infectious process is extremely acute, the disease sometimes running a fatal course in a few hours, yet the body temperature is usually normal or subnormal during the stage of collapse. In this stage, a pronounced disproportion frequently occurs between the temperature and the pulse rate; for example, a temperature of 36° or 37° C. may be accompanied by a pulse rate varying perhaps from 130 to 160 per minute. In contrast to the other infections of the intestine such as tuberculosis, typhoid fever, and bacillary dysentery, there is a marked leucocytosis comparable only to that which is sometimes seen in pneumonia.

Certain features of the disease, such as the short course, the abrupt onset, and the low body temperature, bear more resemblance to the acute intoxications of chemical origin than to the ordinary infectious fevers. During the reaction from the state of collapse the symptoms of toxæmia develop, but the origin of the toxin is not entirely clear. In addition to the hypothetical toxin of the cholera vibrio, the sudden loss of large quantities of fluid[2] from the body gives rise to a considerable mechanical disturbance in the circulation of the blood; it has been suggested that this disturbance might be responsible for all of the symptoms of cholera. However, there are fulminating cases of cholera "sicca," where the loss of fluid is negligible; also, the early relief or prevention of the mechanical disturbance by the administration of fluid to the body, often fails to control the disease.

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[1] Presented at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 8, 1910.

The principal evidence indicating serious metabolic disorder is the rather high percentage of cases which die in uræmia, amounting in some epidemics to 20 per cent (2). Consequently, the treatment of this complication becomes second in importance only to the treatment of collapse. The development of nephritis and uræmia may be dependent both on the toxæmia and on the mechanical disturbance. Mild cases of cholera, with insignificant loss of fluid, not infrequently develop a fatal uræmia. Also, Czerny (3) has shown that when laboratory animals are rapidly deprived of water, recovery takes place on the restoration of fluid, but a temporary albuminuria develops. The following investigation will consider the possible relation between uræmia and certain symptoms of acid intoxication occurring in Asiatic cholera.

The material on which the following data are based consisted of a series of cholera cases occurring almost exclusively among the Malay races in Manila from September, 1909, to January, 1910, inclusive. The total number of cases was distributed with fair uniformity throughout this period. The disease was widely scattered over the city and outlying districts. There was apparently no direct communication between the individual foci of infection, neither was any common source of infection located. The outbreak was rather more endemic than epidemic in character. Of the total of 340 cases, 147 were found dead by the municipal medical inspectors and the remaining 193 were required by the regulations of the Bureau of Health to be transferred to the San Lazaro Hospital. Bacteriologic examination of all cases for the isolation of the cholera vibrio in pure culture was performed by the biological laboratory of the Bureau of Science. Only the cases where the injection of salt solution was indicated, 111 in number, were studied in this investigation. It gives me much pleasure to acknowledge the many courtesies of Dr. A. P. Goff, chief of the San Lazaro Hospital Division of the Bureau of Health.

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[2] The loss of fluid is measurable in liters. The desiccation of the tissues is very general, but the effect on the blood is most noticeable. Rogers (1) found that, instead of the corpuscles forming about 45 per cent of the total volume of the blood, their volume may rise to as much as 60 to 80 per cent, and the fluid content of the blood may be reduced as much as 64 per cent of the total. The viscocity of the blood becomes so great that circulation through the capillaries is effected only with the greatest difficulty. This increased viscocity is probably sufficient to account for the rapid pulse rate, even in the absence of fever. With the continued loss of fluid, the blood pressure in the brachials very commonly falls to zero and the peripheral arteries may remain pulseless for many hours.

In looking for evidences of acid intoxication attention was directed especially to the examination of the urine[3] in regard to: (1) Acetone and acetoacetic acid; (2) the ammonia coefficient; (3) tolerance of the body to alkalies, *i. e.*, the amount of alkali required by the body to render the urine alkaline.

Acetone and acetoacetic acid.—The urine was examined directly, without distillation, for acetone using the iodoform test and the nitro-prussid color reaction. Twenty individuals receiving treatment with sodium chloride were examined. Specimens were obtained from both mild and severe cases including urines voided in collapse, in uræmia and in convalescence. The reactions for acetoacetic acid were somewhat inconclusive. With ferric chloride a definite Bordeaux red color was not obtained, but in seven of the twenty cases a dark red and, in some instances, a slightly brownish-red color was obtained. It is not unlikely that the urinary pigments may have masked the violet shades which are obtained with acetoacetic acid in aqueous solution. Furthermore, the red color faded to a yellow on standing after a few hours; also when the urine was first boiled, no color reaction was obtained. However, one would hesitate to conclude definitely that acetoacetic acid was present, especially as none of the specimens gave a definite reaction for acetone. The absence of acetone seems a little unexpected when we consider that in cholera at least three conditions are present which sometimes give rise to acetonuria, namely, starvation, intestinal disorder, and uræmia.

According to von Noorden (13) acetone and acetoacetic acid usually appear in the urine on the first day of starvation in healthy individuals. Ewing (14) has collected many instances of acetonuria in intestinal disturbances which have been characterized especially as cyclic vomiting and coma dyspepticum. In two cases of uræmia, Lorenz (15) found acetone, acetoacetic acid and β oxybutyric acid.

More extensive observations might offer some explanation for the failure of acetone to appear in the urine; perhaps a larger variety of specimens from different stages of cholera might show that it is not constantly absent.

Ammonia coefficient.—Of course, the ammonia excreted in the urine gives some information as to the amount of acids produced in the body. V. Terray, Vas, and Gara (6) found a pronounced increase in the excretion of ammonia during the stage of reaction and this increase was both relative and absolute, the highest amount recorded being 6.5 grams in one day. In the examination of 28 cases we have found, almost uniformly, an increase in the ammonia coefficient. There were but 6 cases which at any time gave a coefficient of less than 5 per cent, and 3 of these were receiving alkali or acetate in relatively large amounts. In some instances the increase was comparable only to the values obtained in the acid intoxication occurring in diabetes. The data are given in Table VIII.

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[3] No examinations of the blood were attempted. Clinical determinations of the carbon dioxide content of the blood are as yet unsatisfactory. Apparently the normal alkalinity of the blood in cholera is definitely reduced (4). Cantani (5) has even reported an acid reaction of the blood at the end of the life.

Tolerance for alkalies.—If, in cholera, there is an increased production of ammonia for the neutralization of acids, then the administration of alkalies might result, first, in a reduction of the ammonia coefficient, or, second, the amount of alkali which is normally required to render the urine alkaline might be increased.

Preliminary experiments testing the ingestion of sodium bicarbonate by mouth suggested a fairly definite increase in tolerance. The principal source of error attending ingestion experiments would lie in the possibility of a loss of alkali before assimilation. With the expectation of at least partially avoiding such an error, the alkali was given in relatively small quantities and repeated at frequent intervals until the urine became alkaline. Patients were selected who were not in a stage of active diarrhœa; also, only those cases were chosen which were voiding rather freely in order that the results might not be complicated by any marked disturbances in the secretion of urine. Because of these restrictions none of the cases selected showed clinical signs suggesting acid intoxication. In Table I those cases are excluded in which any marked diarrhœa followed the use of the sodium bicarbonate.

TABLE I.—*Showing effect of ingestion of alkalies.*

ONE GRAM SODIUM BICARBONATE EVERY TWO HOURS.

Serial number.	Day of disease.	Condition of patient.	Number of stools.	Total amount of alkali. *Grams.*	Effect on reaction of urine to litmus.	Termination.
1	22	Recovered. One week without symptoms.	0	7	Alkaline for 2 hours.	
2	15	Convalescent (3 days).	0	7	All specimens acid	Recovery.
3	13	Convalescent (1 week).	0	[a]4	do	Do.
4	5	Fair condition	1	7	do	Do.
5	3	Partial collapse	2	7	do	Do.
Control			0	2	Neutral or alkaline for 14 hours.	

TABLE I.—*Showing effect of ingestion of alkalies*—Continued.

FOUR GRAMS SODIUM BICARBONATE EVERY TWO HOURS.

Serial numbers.	Day of disease.	Condition of patient.	Number of stools.	Total amount of alkali.	Effect on reaction of urine to litmus.	Termination.
				Grams.		
7	3	Mild symptoms	0	20	All specimens acid	Recovery.
5	4	In stage of reaction	1	12	Neutral for 2 hours	Do.
6	3	Early uræmia	7	20	All specimens acid	Death.
4	6	In stage of reaction	1	20	do	Recovery.
10	?	Early uræmia	3	28	do	Death.
EIGHT GRAMS SODIUM BICARBONATE EVERY TWO HOURS.						
7	4	Mild symptoms	1	16	Alkaline	Recovery.
8	3	Early uræmia	2	32	All specimens acid	Death.
Normal			0	8	Neutral or alkaline for 7 hours.	
Do			0	8	Neutral or alkaline for 6 hours.	

[a] Bicarbonate discontinued on account of nausea.

In order to eliminate some of the sources of error arising from the ingestion of alkalies, intravenous injection was also tested. In Table I, one patient (Number 8), in addition to the alkali by mouth, received intravenously 40 grams of sodium bicarbonate followed twelve hours later by 10 grams of sodium carbonate, also injected intravenously; the urine remained acid. Intravenous injections of sodium bicarbonate were then taken up systematically.

The majority of the patients were first tested immediately on admission, while in collapse. As a routine, the bladder was emptied by catheter before each injection of alkali. Because of the anuria of cholera there was, in some instances, an unavoidably long interval between the injection of alkali and the first secretion of urine; therefore, these intervals have been included with the other data. The amounts of sodium bicarbonate are stated in terms of the original amount present before sterilization. It is important to note that after sterilization in the autoclave, approximately 0.2 per cent of normal sodium carbonate was present in the solution, being derived from the conversion of the bicarbonate into carbonate by heat.

Precautions were taken not to overlook the excretion of unaltered bicarbonate in the urine. When the reaction of the urine is acid it is evident that there can be no bicarbonate present. In those instances where a neutral reaction was obtained, the urine was tested both before and after boiling to convert any alkali present into a form which would react more readily with litmus. Only the reaction of the first specimen voided after injection is recorded in Table II, but observations were made for at least two days after the last injection. Where "no urine" is recorded, this was determined in each instance by catheterization.

TABLE 11.—*Showing tolerance for intravenous injection of alkali.*

Serial number.	Duration of illness before first injection.	Reaction of urine before injection of alkali.	Amount of alkali, first injection.	Urine.		Alkali.		Urine.		Alkali.		Urine.	
				Interval after alkali.	Reaction to litmus.	Interval between injections.	Amount, second injection.	Interval after alkali.	Reaction to litmus.	Interval between injections.	Amount, third injection.	Interval after alkali.	Reaction to litmus.
	Days. hrs.		*Grams.*	*Hours.*		*Hours.*	*Grams.*	*Hours.*		*Hours.*	*Grams.*	*Hours.*	
14	0 6	X[a]	20		No urine	4	20	15	Acid				
16	0 6	O[a]	20		do	3	40	2	Alkaline[b]	13	30	2½	Neutral.[c]
17	0 8	O	15	3	Acid	3½	20	21	Acid				
18	0 21	Acid	20		No urine	4	20		No urine	4	30	3	Acid.
19	0 8	O	40		do	6	40	7	Acid				
23	0 6	Acid	20		do	3½	20		No urine	5½	20	41	Acid.
24	0 3½	O	20		do	6	20	6	Acid				
25	0 4	Acid	40		do	7	40	17½	Alkaline				
26	0 4	O	40	2	Alkaline	6	40	8	Acid				
27	3 0	O	22		No urine	4	30	6½	do	8	30	3	Faintly acid.
28	0 9	O	30		do	4	30	22	Alkaline[d]				
39	0 7	O	30	1	Alkaline[e]	5	30	1	Acid				
47	0 13	Acid	30	9	Acid								
50	3 0	do	30	16	do								
51	1 0	O	30	40	do								
54	0 6	X	30	5	do								
55	3 0	O	30	9	do	12	30	10	Acid				
56	1 18	O	30	3	do	21	30	2½	do	7	30	2½	Acid

[a] O, signifies no urine, X, that no catheterization was made.

[b] Second specimen 2½ hours later reacted sharply acid.

[c] Remained neutral for 12½ hours after injection and then reacted acid.

[d] Second specimen 8 hours later reacted acid.

[e] Second specimen 2 hours later reacted sharply acid.

The amounts of alkali, administered as shown by the preceding table, varied from 30 to 80 grams, yet in 13 of the 18 cases the urine constantly remained acid. These data are rather definite in view of the ease with which the reaction of the urine can ordinarily be rendered alkaline, for example, by a continued vegetable diet, by the ingestion of certain organic salts, and even by a pure diuresis, such as follows the consumption of sodium chloride (7). Several of the cases also show that the intravenous injection of alkalies, at least in large amounts, will render the urine alkaline. The principal datum, then, which is required to complete this evidence of tolerance is the determination of the effect of the intravenous injection of alkalies on normal individuals, i. e., to determine whether alkalies, in relatively small quantities, when injected intravenously, affect the urine in the same manner as when they are ingested in the alimentary tract.

Absolute conditions of metabolism experiments with exact regulation of the diet were not attempted. Intravenous injections were made in normal adult Malays. The individuals selected were obtained from those classes who live largely on a vegetable diet. The same routine was followed as for the cholera cases. Sodium bicarbonate was given, in 1.5 per cent solution, using a part of the same stock which was employed for the work given in the preceding table. The bladder was emptied by catheter immediately before injection. Either a rather concentrated solution of alkali must be employed or else a relatively large amount of fluid must be introduced. In view of these disadvantages, an extensive series of normal cases was not considered advisable. Three cases only were tested.

TABLE III.—*Intravenous injections of alkali into normal individuals as a control for Table II.*

Number.	Reaction of urine before injection of alkali.	Amount of alkali.	Effect on urine.
		Grams.	
1	Acid	2.0	Reaction constantly acid.
2	do	4.5	Alkaline for 5½ hours after injection.
3	do	5.0	Alkaline or neutral for 11½ hours after injection.

DEGREE OF ACIDITY OF THE URINE.

Titrations of the acidity of the urine could hardly give very important information concerning the acid metabolism. However, in many instances the reaction of the urine not only remained acid after the administration of the alkali, but the acidity was considerably increased, as determined by titration. Table IV shows the maximum acidity found in cases treated with chloride, bicarbonate and acetate of sodium. The estimations were made by titration with $\frac{N}{10}$ sodium hydroxide, with phenolphthaleïn as an indicator, according to the recommendations of Nægeli (8). For convenience, the data are expressed in fractions of a normal solution.

TABLE IV.—*Showing maximum acidity of urine in fractions of a normal solution after intravenous injection.*

Sodium chloride, maximum acidity of urine.	Sodium acetate.		Sodium bicarbonate.	
	Amount, in grams.	Maximum acidity of urine.	Amount, in grams	Maximum acidity of urine.
$\frac{1}{62}$	60	$\frac{1}{15}$	40	$\frac{1}{13}$
$\frac{1}{11}$	15	$\frac{1}{100}$	35	$\frac{1}{14}$
$\frac{1}{25}$	60	$\frac{1}{24}$	70	$\frac{1}{29}$
$\frac{1}{21}$	40	$\frac{1}{12}$	80	$\frac{1}{13}$
$\frac{1}{84}$	80	$\frac{1}{66}$	60	$\frac{1}{84}$
$\frac{1}{20}$	80	$\frac{1}{19}$	40	$\frac{1}{23}$
$\frac{1}{10}$	40	$\frac{1}{17}$	40	$\frac{1}{50}$
$\frac{1}{77}$	80	$\frac{1}{18}$	60	$\frac{1}{18}$
$\frac{1}{62}$	80	$\frac{1}{55}$	60	$\frac{1}{12}$
$\frac{1}{40}$	40	$\frac{1}{14}$	90	$\frac{1}{34}$
$\frac{1}{16}$	60	$\frac{1}{12}$	30	$\frac{1}{35}$
$\frac{1}{50}$	60	$\frac{1}{18}$	30	$\frac{1}{18}$
$\frac{1}{71}$	40	$\frac{1}{18}$	30	$\frac{1}{18}$

GENERAL AVERAGE.

$\frac{1}{30}$	------------	$\frac{1}{20}$	------------	$\frac{1}{20}$

In the preceding table, it is seen that high and low values occur in all three groups of cases. The normal range as stated by Nægeli varies from one one-hundredth to one-thirtieth; in the sodium chloride group there are several instances where the concentration is higher than one-thirtieth normal. The general averages which have been calculated have relatively little significance since many of the cases had received almost sufficient acetate or alkali to neutralize the urine. However, the behavior of the individual cases showed definitely that, *within certain limits,* the injection of bicarbonate or acetate was followed by an increase in acidity of the urine. The first or second specimen voided after injection often showed a normal degree of acidity, but the latter increased rapidly, usually reaching its maximum during the first twenty-four hours after secretion commenced. The decline to normal took place gradually, requiring two or three days. The cause of the increased acidity following the injection of alkali was not determined. One possible factor might be found in the sudden diminution of the albumen content of the urine, which sometimes occurred in cases treated with alkali. This diminution was often quite noticeable in the amount of precipitate obtained on boiling the urine. It is possible, where the albumen content is high, that considerable acid is bound as acid albumen, but with the diminution in the amount of albumen, less acid may be removed during precipitation and becomes available for the neutralization of the alkali.

The presence of alkali albumen in the urine would also be of considerable importance on account of its acid properties. Several specimens of urine were examined for alkali albumen in which the acidity, after the injection of acetate or alkali, was equivalent to one-twentieth of a normal solution or more. Eight samples were tested. In five, no precipitate was obtained on careful neutralization, and in the remaining three only a trace of turbidity appeared, which did not dissolve in excess of alkali. On adding sodium chloride to saturation, three specimens remained clear, four showed a faint trace of precipitate and in one a moderately heavy precipitate appeared. These urines of course contained more or less protein on account of the accompanying nephritis. This last specimen of urine, which precipitated with sodium chloride, gave no precipitate when the acid solution was first heated to boiling and the precipitated proteins removed by filtration.

RELATION OF THE TOLERANCE FOR ALKALIES TO THE ENTERITIS AND TO URÆMIA.

It is of considerable interest to determine whether this tolerance for alkalies depends upon the cholera infection itself or upon the accompanying nephritis. It is important to note that the tolerance apparently increases as the nephritis develops and persists after the enteritis has subsided. In Table II, the only alkaline reactions which were obtained occurred during collapse (cases numbers 16, 25, 26, 28, and 39). Of the patients receiving alkali by mouth, one case (Table I, number 1) was free from symptoms, and examination of the stool no longer showed cholera vibrios to be present; nevertheless, there were indications of a slight tolerance for alkali. A few preliminary tests were sufficient to show at least that nephritis does not always cause a tolerance.

Only four cases were tested, three of chronic and one of acute nephritis. The three chronic cases were voiding freely and showed no definite tolerance. One of these cases was given 4 grams and the other two 8 grams each of sodium bicarbonate by mouth, in one dose, and the urine promptly became alkaline in each instance. However, the case of acute nephritis had developed partial suppression of urine and was excreting about 375 cubic centimeters daily. Fairly definite signs of tolerance were obtained. The ingestion of 32 grams of sodium bicarbonate, in 8-gram doses every three hours, failed to render the urine alkaline. On the day following the administration of alkali, there was no increase in the amount of urine excreted, the twenty-four hour specimen measuring 370 cubic centimeters. On the second day after the first test, an intravenous injection of 1,000 cubic centimeters of a 1.5 per cent sodium bicarbonate solution was given according to the routine used in the cholera cases. Only one alkaline specimen of urine was obtained, and this was the first sample voided after the injection. The acid reaction of the urine returned within two hours after the injection and all succeeding specimens for the next twenty-four hours had an acid reaction. The total volume of urine for the next twenty-four hours increased to 600 cubic centimeters.

While these results are by no means conclusive, yet they might suggest that tolerance was most likely to occur in those cases of nephritis where suppression of urine has developed.

CLINICAL SIGNS OF ACID INTOXICATION.

During the stage of reaction in cholera it is not uncommon to see an almost abnormally bright color of the mucous membranes associated with a type of dyspnœa approaching air-hunger. Such patients usually have either a partial or complete suppression of urine and an increase in the blood pressure which is sometimes as high as 200 millimeters of mercury. In cholera, the symptoms of acid intoxication become so intimately related to those of uræmia that differentiation is hardly possible. Indeed it has been suggested by Senator (9) that uræmia from any cause whatsoever is only an acid intoxication.

INDICATIONS FOR TREATMENT.

The symptoms which indicate an increased production of acid in cholera are as follows:

(1) The tolerance for alkalies is well marked; (2) the ammonia coefficient is almost constantly increased; (3) clinically, there is a stage in which many cases develop an abnormally bright color associated with dyspnœa; (4) as reported in the literature, the blood shows a diminution in alkalinity.

This evidence is hardly sufficient to constitute a proof of acid intoxication. Perhaps the most important point is the increased tolerance for alkalies. Even if we assume that the alkali injected is neutralized in the body by acid, it does not necessarily follow that the acid existed preformed in the body in sufficient quantity to effect neutralization. However, in addition to this group of symptoms, the period of starvation in cholera also offers a possible etiologic factor for the production of acid intoxication. Although the period of starvation is relatively short, amounting only to a few days, yet this means not only absolute deprivation of food, but perhaps a much greater tissue waste than would occur in a normal individual when starved.

There is another explanation depending upon a somewhat different basis which should also be considered. Although alkalies are rapidly excreted by the kidneys in normal individuals, yet the anuria of cholera may permit their retention for a longer or shorter period and thereby possibly give rise to opportunities for the formation of alkali albumen. If we assume, for example, that alkali albumen is formed during a period of anuria, then even after the secretion of urine has commenced, any additional alkali which might be injected could be neutralized in the body by the acid properties of the alkali albumen already formed. The conditions bearing upon the possibility of the formation of alkali albumen were as follows: The concentrations of bicarbonate before injection varied from 1 to 2 per cent. Estimating the quantity of the blood as one-twentieth of the body weight in cholera patients, the maximum concentration of alkali after injection would be about 0.8 per cent. In certain cases where the loss of fluid had been replaced by sodium chloride solution, the quantity of blood may be estimated as normal, and the minimum concentration calculated for the 1 per cent solution of bicarbonte would be about 0.3 per cent after injection. The duration of the period of anuria was rather long in some instances, for example, fifty and forty hours in numbers 23 and 51, Table II. On the other hand, several cases which showed a definite tolerance were excreting rather freely, for example, numbers 54 and 56 in Table II. Hence, it is hardly probable that the formation of alkali albumen could be the sole factor in explaining the differences between the control individuals and the cholera cases.

Lastly, it may be noted that the condition known as acid intoxication is but imperfectly understood and that there is no standard method for its diagnosis.

The essential feature to be determined in regard to treatment, is whether this apparent tendency toward acid intoxication is a protective mechanism which should be encouraged, or whether it is a deleterious condition which should be opposed. During the intense cyanosis of collapse, the use of alkalies, theoretically, has relatively little value. On the other hand, the stage of reaction constitutes an entirely different condition. In the administration of alkalies the principal points to be determined are, namely: (1) How early does the tolerance for alkalies develop and at what stage should their administration be commenced? (2) In what form should alkali be employed and in what amount may it be used?

The symptoms of acid intoxication become more pronounced as the disease progresses. The tolerance for alkalies apparently did not reach its height before the third or fourth day. The ammonia coefficient was usually not excessively increased during the first and second day. During collapse there was intense cyanosis and the bright, flushed color did not appear until patients were well along in the stage of reaction. As to the period at which the administration of alkalies must be begun in order to prevent the appearance of acid intoxication, this must be determined by more or less empiric methods.

In the treatment of acid intoxication there are, apparently, two objects to be accomplished, namely, (1) the neutralization of acid, and, (2) the removal of carbon dioxide. Three groups of chemicals may be considered for this purpose: The normal carbonates and hydroxides, the bicarbonates, and certain neutral salts of the organic acids.

Of the first group, normal sodium carbonate is most commonly employed and, of course, without preliminary alteration combines with carbon dioxide and neutralizes acid. The bicarbonates, being saturated with carbon dioxide, can only neutralize acids, while the organic salts, such as the acetates and citrates, can do neither. However, both the organic salts and the bicarbonates are converted in the body, in part at least, to the carbonate. The ultimate decision as to the most suitable form of chemical to be employed may be found to vary according to the stage of the disease in which its administration is commenced. We have tried normal sodium carbonate, sodium bicarbonate, and sodium acetate from the three groups just mentioned. Normal sodium carbonate, in relatively small quantities, has long been recommended for use in cholera, but no reports have been found as to the effect of this treatment. Apparently the largest amount which has been used is that recommended by Manson,(10) who suggests a concentration of 60 grains to the quart, injecting about 2 to 3 quarts of fluid, making a maximum of about 12 grams of sodium carbonate. This solution is apparently intended to be used for the treatment of collapse.

EFFECTS OF ALKALIES IN ASIATIC CHOLERA.

In testing the normal carbonate, a slightly stronger solution than that used by Manson was prepared, namely, 0.5 per cent each of sodium chloride and sodium carbonate, and used in two cases *in extremis*. Following the usual routine, 2 liters of fluid were employed and in each instance death occurred five hours after the injection.

The first case was one which had been in uræmia for three days. The injection was followed, after about four hours, by slight convulsions, but it is impossible to say whether or not they were caused by the alkali. The urine did not become alkaline. The second case was in total collapse and did not respond to the injection. No urine was secreted. There was a slight muscular rigidity which lasted a few minutes. The suppression of urine could hardly have been responsible for this rigidity, since the total duration of illness was less than one day. No changes in the erythrocytes occurred in either case.

Because of the apparent tendency to cause convulsions, the normal carbonate was discarded and a small group of cases was tested, using sodium bicarbonate in varying amounts and concentrations, but always commencing the injections during the stage of collapse. In the majority of cases, two liters of fluid have been given at each injection. Three concentrations of sodium bicarbonate were employed, namely, 1, 1.5, and 2 per cent. One-half per cent of sodium chloride was added to the 1 per cent solution, but the two stronger solutions were made up without the addition of any other salts.

The preparation of sterile sodium bicarbonate in large quantities (20 to 40 liters) offers some difficulties because of the instability of this salt at the temperatures required for sterilization. The normal carbonate is rapidly formed even at 70° C. When solutions are heated in the autoclave a considerable portion of the bicarbonate is changed permanently to the normal carbonate. All of the concentrations used were sterilized by heat except some of the 2 per cent solutions, which were filtered through porcelain.

Estimation of the amount of change occurring during sterilization was made by titration against $\frac{N}{10}$ hydrochloric acid with phenolphthaleïn, at a temperature of 0° C. At any temperature a solution of neutral alkali carbonate is hydrolyzed according to the equation $Na \cdot Na\ CO'_3 + H \cdot OH' \rightleftharpoons Na \cdot OH' + Na \cdot HCO'_3$ At ordinary temperatures a sharp end-point can not be obtained, but at 0° the solution may be titrated against hydrochloric acid with phenolphthaleïn to a fairly exact equilibrium. The concentration of the hydrogen ions from the dissociation of sodium bicarbonate is too low to affect the indicator and the reaction takes place just as if the latter were not present; the amount of acid required for neutralization represents, therefore, only half of the alkali present as normal carbonate. Sterilization was carried on for one hour at 7 pounds pressure in an autoclave connected with live steam. By keeping conditions constant with regard to pressure and duration of heating, successive lots of solution were obtained which were fairly constant in composition.

According to the basis of calculation just outlined the average amount of change was as follows:

$NaHCO_3$, in grams, per 100 cubic centimeters before sterilization.	After sterilization.			
	Cubic centimeters of $\frac{N}{10}$HCl required to neutralize 10 cubic centimeters of alkali.	Per cent of $NaHCO_3$ converted to Na_2CO_3.	Grams $NaHCO_3$ per 100 cubic centimeters.	Grams Na_2CO_3 per 100 cubic centimeters.
1.0	1.8	30	0.7	0.19
1.5	2.4	27	1.1	0.26

These results do not represent a chemical equilibrium but show the progress of the reaction under certain given conditions. The fact that a relatively large amount of bicarbonate remained unchanged notwithstanding the high temperature, might be accounted for by the use of pressure during sterilization which would prevent the evolution of steam from the solution.

All the patients included in Table V, except numbers 27 and 39, were admitted in complete collapse; one case (number 27) was complicated with an acute, bloody dysentery. No detailed classification of the condition of the cases was attempted other than the separation into partial and complete collapse. Physical examination is hardly a satisfactory basis for the comparison of different cases; thus the records of the pulse, temperature, blood-pressure, respiration, and the other evidences of loss of fluid may not differ markedly in cases which evidently may have a widely different prognosis. Furthermore, cases which to all appearances are very similar may behave rather differently under the same treatment.

Seven of these 14 cases died during collapse. This is not a proportionately greater death rate from collapse than occured in the control series treated with sodium chloride; yet observation of the individual cases seemed to indicate that in some instances they responded less promptly to the alkaline solution.

The use of organic salts affords certain distinct theoretical advantages. On injection, these neutral salts possess only the properties of salt action and might be equally efficient with sodium chloride for the treatment of collapse. However, subsequently after oxidation they would afford the properties of an alkali and also of a diuretic. Furthermore, a salt can be chosen which is chemically stable during sterilization, thereby avoiding the formation of the hydroxide or normal carbonate such as occurs in the sterilization of sodium bicarbonate.

The group of cases recorded in Table VI was tested with sodium acetate. The acetate was selected in preference to the citrate because of the solubility of calcium acetate. Busquet and Pachon (11) have reported that the citrates, the normal carbonates and that group of salts which precipitates calcium are more deleterious in their action on the heart than those acids, the calcium derivatives of which are soluble. The concentrations given in Table VI are calculated for the crystallized salt, the 1.5 per cent solution representing approximately 0.9 per cent and the 2 per cent solution 1.2 per cent of the anhydrous salt.

The patient (number 32) who died in uræmia represented a type of those cases which develop only a mild enteritis, but terminate in a fatal uræmia.

This patient, on admission, received 30 grams of sodium acetate intravenously. The first laboratory examination did not show cholera vibrios in the stool. The condition of the patient appeared altogether favorable, but on the fifth day, slight symptoms of uræmia developed in addition to the partial suppression of urine which had been present, and a second examination of the stools showed the presence of cholera vibrios. On the sixth day, 30 grams of sodium bicarbonate were injected intravenously. The secretion of the urine started promptly and in the following fifteen hours 600 cubic centimeters were excreted, an amount equal to the total volume for the five days previously. The urea content was 7.8 grams as compared with 1.9 grams for the same volume of urine excreted before the injection of alkali.

In another instance the acetate was discontinued after the first injection. Symptoms of uræmia developed rather suddenly, and injection of sodium bicarbonate was commenced on the third day. In the remaining twelve days of life, a total of 180 grams of sodium bicarbonate was

TABLE V.—*Cases treated during collapse with sodium bicarbonate.*

Serial number.	Age.	Duration of illness.		Cubic centimeters of urine on admission.	First day.			Second day.			Amount of urine, in cubic centimeters.			Reaction of urine to litmus.	Total amount of alkali, in grams.	Length of course of the disease.		Termination.
					Sodium bicarbonate.		Cubic centimeters of urine.	Sodium bicarbonate.		Cubic centimeters of urine.	Third day.	Fourth day.	Fifth day.					
					Percent.	Amount, in liters.		Percent.	Amount, in liters.									
		Days.	*hrs.*													*Days.*	*hrs.*	
11	25	0	8	7	1	4	0								40	0	16	Death; collapse.
14	25	0	6	X[a]	1	4	0			380	1,580	1,600	1,690	Acid	40	15	0	Recovery.
16	30	0	6	0	1 2	2 3½	40			1,020	575	650	1,065	Alkaline	90	19	0	Do.
17	35	0	2½	0	1	3½	2			540	505	880	1,270	Acid	35	18	0	Do.
18	19	0	21	1	1 2	4 1½	100			0				do	70	1	16	Death; collapse.
19	38	0	8	0	2	4	40			700	1,740	1,050	330+	do	80	6	0	Death; pneumonia.
21	40	0	6½	0	2	3½	0	2	1½	0					100	2	0	Death; collapse.
23	56	0	6	10	1	6	0	(b)	(b)	0	85	815	2,170	Acid	60	17	0	Recovery.
24	28	0	3½	0	1	4	10			135	20	655	710	do	40	17	0	Do.
25	50	0	4	5	2	4	0			5				Alkaline	80	0	24	Death; collapse.
26	18	0	4	0	2	2	10			30				do	40	0	21	Do.
27	30	3	0	0	1½	5½	140							Acid	82	4	0	Death; enteritis.
28	19	0	6	0	1½	4	0			60	255	1,030	2,650	Alkaline	60	16	0	Recovery.
39	21	0	7	0	1½	4	135			40	845	1,530	2,180	do	60	17	0	Do.

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[a] No catherterization.

[b] Normal salt solution, 2 liters.

TABLE VI.—*Cases treated with sodium acetate.*

Serial number.	Age.	Duration of illness.	Cubic centimeters of urine on admission.	First day.			Second day.			Amount of urine, in cubic centimeters.			Reaction of urine to litmus.	Total amount of acetate, in grams.	Length of course of the disease.	Termination.
				Acetate.		Cubic centimeters of urine.	Acetate.		Cubic centimeters of urine.	Third day.	Fourth day.	Fifth day.				
				Per cent	Amount, in liters.		Per cent.	Amount, in liters.								
		Days. hrs.													*Days.*	
IN PARTIAL COLLAPSE.																
32	29	0 7	0	1.5	2	2			50	270	200	[a] 80	Acid	30	7	Death; uræmia.
33	25	0 14	0	2	2	0			830	1,050	1,300	1,300	do	40	10	Recovery.
37	40	0 10	0	2	[b] 4	0			0	70	140	1,800	do	80	12	Do.
43	27	0 10	0	2	2	0			110	465	1,580	1,700	do	40	13	Do.
44	30	0 7	0	2	[b] 4	0			330	140			do	80	4	Death; enteritis.
38	18	3 0	0	([b])		0	2	4	0	280	830	720+	do	80	9	Do.
IN COMPLETE COLLAPSE.																
30	28	0 18	0	1.5	2	0	1.5	2	0	390	980	1,450	Acid	60	13	Recovery.
31	57	0 6	0	1.5	4	0			20	([c])	([c])		do	60	9	Do.
34	60	0 7	0	2	4	0			100	950	1,400	1,000	do	80	9	Do.
35	55	0 24	0	2	[b] 4	0			10	1,300	560	650	do	80	9	Death; pneumonia.
36	40	0 10	x	2	[b] 4	0			0	15			Alkaline	80	3	Death; enteritis.
42	28	0 4	0	2	[b] 4	0			0	740	2,250	1,280	Acid	80	10	Recovery.
46	22	0 3	0	2	4	5	([b])		0	260	([c])	2,100	do	80	14	Do.
49	50	0 17	10	2	2	100	2	2	30	440	1,250	470	do	80	8	Death; enteritis.

[a] On the sixth day this patient received 30 grams of sodium bicarbonate intravenously.

[b] Two liters of isotonic salt solutions were also given following the injections of sodium acetate.

[c] Involuntary.

There were also 4 cases dying in collapse after an illness of less than two days and a fifth case which is described in the text.

injected. The secretion of urine commenced promptly after the first injection and continued until death. The blood-pressure, after the first injection, fell from 140 to 115 millimeters of mercury. The color continued very bright and the respirations were deep, but the rate was normal. On the eleventh day of the disease, examinations of the stools showed them to be free from vibrios. Death occurred four days later. At autopsy the small intestine was found to be almost gangrenous. There was no attempt at reparation of the intestine, the lower half of the ileum being almost entirely denuded of the mucosa. In some areas, only the muscularis and serous coats remained.

The total duration of the disease in this patient is in marked contrast with the series of cases treated with sodium chloride in which seven days was the maximum course for the fatal cases.

If the percentage of mortality is considered in this group, it must be noted that four of the cases were almost moribund on admission. Occasionally, the secretion of urine did not commence very promptly after the injection of acetate. After secretion was established, the amount voided was usually about normal, although the nitrogen output as judged by the urea content was frequently rather low. However, some of the cases with low urea output made very satisfactory recoveries. Although in normal individuals acetates are oxidized almost completely to alkali, yet it does not follow that cholera patients would effect the complete oxidation of excessively large quantities of acetate. However, no acetate could be detected in the urine by the ferric chloride or ethyl acetate tests, although these reactions were rather unsatisfactory when applied to urine. In three cases where the acetate was given in 80-gram quantities, the distillation of the strongly acidified urine showed only a trace of volatile acid.

A third group of cases was studied, abandoning any attempt at a routine for all patients. The general plan of treatment was to use sodium chloride solution for the stage of collapse, starting the sodium bicarbonate as soon as the stage of reaction commenced. The bicarbonate was used when indicated for patients who did not go into collapse, its indication being judged by the dyspnœa, the flushing of the cheeks and mucous membranes, the suppression of urine and the rise of blood pressure. For those cases where the loss of fluid was moderate and it seemed probable that only one or two injections would be required, the bicarbonate was used for the first injection.

In addition to the cases recorded in Table VII, there were also five other cases which were placed in the bicarbonate series on admission. These died under sodium chloride treatment before the stage of reaction was reached; consequently they received no alkali, as there was no definite indication for its use. In the outline which follows later, these five cases are included with the number of deaths from collapse occurring under alkaline treatment, for otherwise the alkali series would represent selected cases.

TABLE VII.—*Cases treated both with sodium chloride and sodium bicarbonate.*

IN PARTIAL COLLAPSE.

Serial number.	Age.	Duration of illness.		Cubic centimeters of urine on admission.	First day.			Second day.			Third day.			Amount of urine, in cubic centimeters.		Reaction of urine to litmus.	Total amount of alkali, in grams.	Course of the disease.	Termination.
					Sodium bicarbonate.		Cubic centimeters of urine.	Sodium bicarbonate.		Cubic centimeters of urine.	Sodium bicarbonate.		Cubic centimeters of urine.	Fourth day.	Fifth day.				
					Per cent.	Amount, in liters.		Per cent.	Amount, in liters.		Per cent.	Amount, in liters.							
		Days.	*hrs.*															*Days.*	
47	30	0	8	40	1.5	2	100			1,240			4,660	3,880	1,240	Acid	30	8	Recovery.
48	60	0	9	0	1.5	[a]2	0	1.5	2	0			[b]215	600	760+	Alkaline	90	15	Do.
50	25	2¼	0	80	1.5	2	0			320			2,750	2,800	960+	Acid	30	15	Do.
52	45	0	2	0	(c)		20			100	1.5	2	230	1,290	3,090	do	30	21	Do.
55	58	0	11	0	(c)		0			10			13	[d]135	1,580	do	60	17	Do.
56	32	0	9	0	(c)		20	1.5	2	15	1.5	4	1,820	6,630	2,840+	do	90	6	Death; pneumonia.
59	23	2	0	×	1.5	2	0			1,050			1,240	Convalescent.		do	30	10	Recovery.
63	30	0	16	×			0	1.5	2	105	1.5	2	370			do	60	3½	Death; enteritis.

IN COMPLETE COLLAPSE.

51	49	1	0	0	1.5	2	0			68			1,460	1720	1,440	Acid	30	20	Recovery.
54	19	0	6	×	1.5	2	20			1,920			1,460	1230	1,055	do	30	20	Do.
57	48	0	9	0	(c)		0	(c)		0	1.5	2	140	[d]365	(f)	do	90	9	Death; enteritis.
58	65	1	0	×	(c)		0	1.5	2	0	1.5	2	175	240	1,000	do	60	9	Recovery.
60	30	0	9	0	(c)		0	[e]1.5	2	0	(a)		30	0	10	do	30	4	Death; enteritis.

61	30	0	14	×	1.5	2	0	1.5	2	0	----------	----------	0	[b] 0	2,730	----do----	90	17	Recovery.
62	30	0	7	0	(c)	----------	0	1.5	2	1,320	----------	----------	2,350	1990	1,220	----do----	30	11	Do.
64	40	1	0	0	(e)	----------	0	(a)	----------	0	1.5	2	140	[b] 780	1,510	----do----	60	15	Do.
65	37	3	0	×	1.5 (c)	2	50	----------	----------	----------	----------	----------	----------	----------	----------	----do----	30	4	Death; collapse.

[a] Two injections isotonic salt solutions 2 liters each.

[b] Two liters of 1.5 per cent of sodium bicarbonate.

[c] Hypertonic salt solution 2 liters.

[d] Four liters of 1.5 per cent of sodium bicarbonate.

[e] Three injections isotonic salt solutions 2 liters each.

[f] Involuntary.

This group of cases showed that the injection of bicarbonate, in sufficient quantity, was followed by an active secretion of urine. In one case (number 56) excessive amounts were voided, more than 6 liters being excreted in twenty-four hours. The urine secreted after the injection of alkali differed in several respects from that obtained after the injection of the chloride; after the use of the bicarbonate, both the quantity of urine and also the urea content (see Table IX) rose rapidly to normal. The acidity as determined by titration was sometimes increased. Not infrequently the amount of albumen diminished rapidly and the urines became albumen free at an early period.

One patient (number 50) in this series was of special interest.

He was admitted after an illness of two and one-half days. The symptoms of uræmia were fairly definite. The suppression of urine was absolute. Respiration was natural. The cheeks were flushed and the mucous membranes were bright pink in color. The pulse was full and bounding and the blood pressure measured 175 millimeters of mercury. Thirty grams of sodium bicarbonate were injected intravenously. The bright color of the mucous membranes persisted, but the tension of the pulse diminished rapidly and, after an interval of ten hours, the blood pressure had fallen to 135 millimeters. Sixteen hours after the injection, the secretion of urine commenced. The amount was small at first but steadily increased, and a prompt recovery followed.

In another patient (number 48) the anuria persisted until the third day. The secretion of urine finally commenced eighteen hours after a subcutaneous injection[4] of 30 grams of sodium bicarbonate. The first specimen of urine was entirely colorless and contained no trace of urea or ammonium salts. However, there was considerable alkali present, amounting to about one-fifth of a normal solution, which was present both in the form of carbonate and bicarbonate. The second specimen, a few hours later, contained a little pigment and a trace of urea, while the third specimen was almost normal.

In addition to following the reaction of the urine, estimations of the ammonia coefficient[5] were made as a further aid in determining the most desirable dosage of alkali. High coefficients were found, not only in the cases treated with chloride solutions, but these high values sometimes persisted even after the administration of relatively large amounts of alkali. The quantities of alkali stated in Table VIII were injected before the urine was voided.

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[4] The danger of abscess formation and necrosis after the subcutaneous injection of alkalies has been emphasized repeatedly, but this method may occasionally be justifiable in the extreme conditions of cholera. In five instances where the available number of superficial veins was limited, sodium bicarbonate was injected subcutaneously in 1.5 per cent concentration. In no instance was there any evidence of necrosis or abscess formation. Two of these cases were in an extreme condition and it was expected that a second injection of alkali would be required. A few hours after the injection, both patients complained of muscular cramps throughout the body. The secretion of urine commenced without further use of alkali.

[5] It gives me much pleasure to acknowledge the very helpful coöperation of Mr. George F. Richmond, chief of the chemical laboratory, Bureau of Science. These determinations were made under his direction, by Folin's (12) method.

TABLE VIII.—*Showing ammonia coefficient under different conditions.*

CASES TREATED WITH SODIUM CHLORIDE.

Serial number.	Amount, in grams.	Day of disease.	Nitrogen as ammonia in per cent of total nitrogen.	Day of disease.	Nitrogen as ammonia in per cent of total nitrogen.	Termination.
8		Third	15.8	Seventh	27.3	Recovery.
13		Second	12.5	Third	9.2	Do.
15		First	9.4	Second	9.9	Do.
20		do	2.5	do	20	Death; collapse.
22		Fourth	37.9	Sixth	12.5	Death; uræmia.
29		Third	0.8			Recovery.
40		Third[a] Fourth Fifth			12.2	Death; uræmia.
41		Fourth	8.5			Recovery.
53		Third	25.7	Fourth	21.7	Do.
66		Second	4.2			Death; collapse.

CASES TREATED WITH SODIUM ACETATE.

Serial number.	Amount, in grams.	Day of disease.	Nitrogen as ammonia in per cent of total nitrogen.	Day of disease.	Nitrogen as ammonia in per cent of total nitrogen.	Termination.
30	60	Fourth	8.3			Recovery.
31	60	do	7.4			Do.
33	40	First	12.5	Second	16.3	Do.
34	80	Fifth	6.3			Do.
38	40	do	15.6			Death; enteritis.
42	80	Fourth	1.4			Recovery.
43	80	do	10.0			Do.

CASES TREATED WITH SODIUM BICARBONATE.

Serial number.	Amount, in grams.	Day of disease.	Nitrogen as ammonia in per cent of total nitrogen.	Day of disease.	Nitrogen as ammonia in per cent of total nitrogen.	Termination.
14	40	Second	10.8	Third	5.4	Recovery.
16	70	do	1.2	Fourth	7.3	Do.
17	35	do	16.1	Third	12.8	Do.
18	70	do	5.3			Death; collapse.
19	80	First	3.6	Second	5.5	Death; pneumonia.
23	60	do	40.7	Fourth	42.0	Recovery.
24	40	do	5.7	do	7.5	Do.
27	52	Second	5.9			Death; enteritis.
28	60	do	8.2	Fourth	8.5	Recovery.
48	30	Fourth	18.0			Do.
50	30	do	16			Do.

[a] Composite sample.

In the bicarbonate series, with one exception, only those solutions were free from normal carbonate which were sterilized by filtration without heat. There is the possibility, of course, that in the heated solutions the active agent was not the bicarbonate, but the normal carbonate which was also present. However, this explanation is excluded, first by the similarity in the action of the neutral sodium acetate as compared with the bicarbonate, and, secondly, by the fact that in two cases (numbers 27 and 28) the normal carbonate was removed from the bicarbonate solution by the following procedure:

A 2 per cent solution of sodium bicarbonate was sterilized by heat and the normal carbonate removed by adding an excess of normal hydrochloric acid. Sufficient acid was added to reduce the content of sodium bicarbonate to 1.5 per cent and the solution was then allowed to stand several hours to permit the escape of the undissolved carbon-dioxide, but no special precautions were taken to remove the carbon dioxide in solution.

CASES TREATED WITH SODIUM CHLORIDE.

For comparison with the cases treated with alkali and acetate, a duplicate series was carried out, using the ordinary treatment with sodium chloride. The general nature and severity of the cases varied comparatively little throughout the period of investigation, thereby facilitating the division of the patients into fairly comparable groups. Of the total of 111 cases investigated, the first 20 were treated with Ringer's solution. In the remaining 36 cases of the control series, sodium chloride alone was used, and these cases were distributed uniformly throughout the series. Both hypertonic (1.3 per cent) and isotonic (0.85 per cent) salt solutions were employed.[6] The following outline gives a summary of the causes of death in the group of cases treated with sodium chloride in comparison with those receiving alkali.

Treatment.	Number of cases dying in—		
	Collapse or enteritis.[a]	Pneumonia.	Uræmia.
Chloride	30	2	8
Acetate or bicarbonate	24	3	1

[a] The term "enteritis" is used to designate those cases which died from the toxæmia of the cholera infection in distinction from the toxæmia of uræmic origin.

The causes of death, usually, were rather sharply differentiated. The uræmic cases, in addition to dyspnœa and suppression of urine, showed at least a normally bright color and usually considerable elevation of the blood pressure, which sometimes registered as much as 140 to 180 and even 200 millimeters of mercury. Constipation in these cases was not uncommon in the later stages of the disease. Those patients who lived three or four days, but with cyanosis, soft pulse, and normal or subnormal blood-pressure, are considered as having died of enteritis rather than uræmia, *even though respiration* was labored and the suppression of urine was absolute. The initial loss of fluid by rectum in these cases might account for the absence of urine; also in these cases the diarrhœa frequently continued until death.

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[6] The conclusions in regard to the relative value of isotonic and hypertonic salt solutions for the treatment of collapse will appear in this number of the *Journal*.

In reviewing the two groups it is noteworthy that the majority of patients who recovered under the sodium chloride treatment did not develop absolute suppression of urine for as long a period as twenty-four hours. However, in the alkali series, in addition to those which did not develop complete suppression, a considerable number recovered even after two days of absolute suppression.

The following outline gives a summary of the cases which recovered.

Treatment.	Number of days of absolute suppression.			
	None.	One.	Two.	Three.
Chloride	9	6	1	0
Bicarbonate and acetate	7	12	7	1

The final results were as follows:

Treatment.	Number of cases.	Deaths in uræmia.	Total number of deaths.	Number of recoveries.
Chloride	56	8	40	16
Bicarbonate and acetate	55	1	28	27

Calculation of percentages upon such a small group of patients could have little significance. However, it is noteworthy that the increased number of cases recovering under the alkaline treatment corresponds roughly to the number of deaths from uræmia under the sodium chloride treatment. Assuming that alkalies affect uræmia only and have no influence upon collapse, then the theoretical limits of this increase would be the percentage of cases which ordinarily die in uræmia. Of the 56 cases treated with sodium chloride, 8, or 14 per cent, died in uræmia. This corresponds closely to the conditions in India where Rogers (1) reports an incidence of 13.2 per cent of uræmia in cholera.

SUPPRESSION OF UREA.

After secretion of the urine was established, determinations of the urea content showed a suppression of urea somewhat comparable to the suppression of urine. In the following table, the determinations were made by the sodium hypobromite method and therefore include the ammonium salts as well as the urea. The analyses were at first made on twenty-four hour specimens of urine, but, after a marked suppression of urine, a sudden increase in the urea content frequently occurred such as would be overlooked in estimations of the total urea excreted per day. For example, the first 100 cubic centimeters of urine voided after a period of suppression might contain only 0.3 per cent of urea. For the remaining twenty-four hours, perhaps a liter of normal urine might be voided. It was necessary to examine each successive specimen separately in order to detect these critical changes.[7]

The percentage of urea, apparently, was almost independent of the quantity of urine which was voided, and, at least as shown by Table IX, the sudden increase in percentage was not due to a diminution in the volume excreted, but was rather accompanied by an increase in volume. The changes in the urea content did not consist in fluctuations from small to large amounts, but the increased outputs were maintained.

TABLE IX.—*Showing changes in excretion of urea.*

Serial number.	Treatment.	First day.	Second day.	Third day.	Fourth day.	Fifth day.	Sixth day.
		Per cent.	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*
9	Sodium chloride	0.4	0.5	0.4		1.2	
12	do	2.8		3.5			
13	do	0.4	0.35	1.1	1.5	2.4	
15	do	1.0	1.8				
22	do		0.2	0.3	0.25	0.5	0.3
53	do	0.1	0.25	0.6	0.5		
52	Sodium bicarbonate, 30 grams.	0.05	0.75	1.5			

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[7] The accurate collection of an extensive series of specimens in the midst of an epidemic was made feasible by the very excellent supervision of Miss A. E. McEvoy, Mrs. K. E. Taulbee, and Miss B. M. Gertsch, the nursing staff of San Lazaro Hospital.

TABLE IX.—*Showing changes in excretion of urea*—Continued.

Serial number.	Treatment.	Urea.	Interval.	Urea.	Interval.	Urea.	Interval.	Urea.	Interval.	Urea.
		Per ct.	*Hours.*	*Per ct.*	*Hours.*	*Per ct.*	*Hours.*	*Per ct.*		*Per ct.*
20	Sodium chloride	0.1	5	0.1	5	0.1	6	0.1	------	------
29	do	0.4	19	0.4	Quantity about 2.5 liters daily.				Recovery	------
40	do	0.2	13	0.1	12	0.15	24	0.4	------	------
45	do	0.15	5	0.15	4	0.2	3	0.5	24 hours	0.4
19	Sodium bicarbonate, 80 grams.	0.05	16	1.2	24	1.8	------	------	After 3 days.	1.4
47	Sodium bicarbonate, 30 grams.	[a]0.3	19	1.3	------	------	------	------	------	------
48	Sodium bicarbonate, 90 grams.	None	17	0.25	8	0.4	------	------	------	------
50	Sodium bicarbonate, 30 grams.	[a]0.05	9	0.4	9	1.3	------	------	------	------
54	do	0.05	2½	0.5	1	0.8	1½	1.3	------	------
56	Sodium bicarbonate, 60 grams.	0.6	6	1.3	------	------	------	------	------	------
33	Sodium acetate, 40 grams.	0.05	6	0.35	8	2.2	------	------	------	------
35	Sodium acetate, 80 grams.	0.05	24	1.4	------	------	------	------	------	------
37	do	0.4	17	1.4	------	------	------	------	------	------

[a] Before injection of alkali.

In those cases in the sodium chloride group in which the percentage of urea was definitely lowered, the return to normal took place gradually (cf. especially numbers 53, 20, 40, and 45), while in the alkali group, a sudden increase in the output of urea was frequently noted (e. g., numbers 19, 47, 50, and 54). It would be of interest to determine whether the suppression of urea was due to the inability of the kidney to excrete urea or whether the metabolism was at fault and the organism unable to produce urea. It would seem a little unusual for the kidney to excrete fluid and salts freely, and yet be limited to subnormal amounts of urea. *A priori*, one would expect that the tolerance for alkalies is produced by a disturbance in metabolism rather than by a local lesion of the kidney. Assuming the presence of an acid intoxication, it might be expected that in the cases treated without alkali the nitrogen, which would ordinarily go to form urea, is utilized for the neutralization of acids, but in the presence of alkali it is no longer needed for this purpose and is excreted as urea.

CONCLUSIONS CONCERNING TREATMENT.

The behavior of these various groups of cases has led to the following conclusions:

1. The choice of alkali for treatment may vary somewhat in the different stages of cholera. The chief advantage of the normal carbonate would depend upon its ability to absorb carbon dioxide, but apparently few deaths occur primarily from failure of the internal respiration.

2. Sodium acetate may have some advantages, especially for the stage of collapse. As much as 80 grams within twenty-four hours have been injected, but perhaps this amount is slightly excessive in certain cases.

3. As a general routine, sodium bicarbonate has been the most effective of the three salts. Its administration in collapse has several advantages and, in selected cases, concentrations of 1 or 1.5 per cent may be used. A weaker solution could probably be chosen which would be suitable for routine use in all cases of collapse. Early in the stage of reaction, at least as much as 60 grams may readily be given within twenty-four hours. The most important indication for discontinuing its administration is the development of muscular cramps or twitchings. These symptoms may appear, although the urine remains acid, and may be considered as a reaction to the alkali. Several cases in which excessive amounts of alkali were tolerated without the appearance of this symptom, terminated unfavorably. There was a wide variation in the amount of alkali which resulted in the production of muscular contractions. The quantity apparently varied in direct proportion to the severity of the disease although Loeb (16) has shown that the precipitation of the calcium salts by carbonates gives rise to muscular contractions. If administration of alkalies is delayed until uræmic symptoms develop, secretion of urine follows promptly after injection of sodium bicarbonate, but the final termination is usually unaltered.

4. In no case was the urine kept constantly alkaline. Indeed, in the majority of cases an alkaline reaction was never obtained, and it is difficult to conjecture what the effect might be of maintaining a constantly alkaline urine throughout the course of the disease.

5. The most important single factor in determining the amount and frequency with which alkali should be injected is the quantity of urine excreted. Sodium bicarbonate in 1.5 per cent solution in 2-liter quantities has been injected as soon as patients come out of collapse and repeated at twelve to twenty-four hour intervals until a free secretion of urine follows. Aside from mild convulsions, the only other untoward symptoms following the injection of alkali was a temporary hæmaturia. This occurred in 3 of the 55 cases. It was slight in amount and persisted for from two to four days.

6. In comparing the two groups of cases, namely, those treated

with chloride and those with alkali, the most important difference is the absence of uræmia in the bicarbonate series. As a rule, morphia failed to quiet patients when the stage of uræmia had developed. However, after the injection of alkali, the respiration improved and the restlessness of the patients disappeared. Observation of the individual cases sometimes showed a sudden improvement following the injection of alkali. The value of the injection of alkalies is seen most clearly in that class of cases which have only mild symptoms of cholera, but which nevertheless develop a fatal uræmia.

7. In the specific treatment of cholera, there are several distinct pathologic conditions which are commonly present and, consequently, no one treatment can meet them all. The treatment of the toxæmia, which is the most important factor, is not under satisfactory control. The effect of fluid on the relief of mechanical conditions in the stage of collapse is well established. Symptoms of acid intoxication and the development of uræmia during the stage of reaction did not occur (except in one instance) in a group of fifty-five cases treated with acetate or bicarbonate of sodium.

GENERAL SUMMARY.

1. Examination of the urine in cholera showed an almost constant increase in the excretion of ammonia.

2. Cholera patients showed a definite tolerance to alkalies, a considerable excess of sodium bicarbonate being required to render the urine alkaline as compared with normal individuals. Within certain limits, the administration of alkalies not only failed to render the urine alkaline, but its acidity was even increased, as measured by titration. Following the injection of alkalies, there was sometimes a sudden and marked increase in the excretion of urea.

3. The early administration of alkalies practically eliminated death from uræmia.

The most important findings are the tolerance for alkalies and the change in the course of the disease. This tolerance may be dependent either upon the cholera infection, or upon the accompanying nephritis; apparently it is related more closely to the uræmia than to the enteritis. The condition will be of more general interest if it proves to be present in uræmia from other causes than if it is specific for cholera.

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EFFECT OF THE CONCENTRATION OF SOLUTION IN THE TREATMENT OF COLLAPSE IN ASIATIC CHOLERA.

By Allan J. McLaughlin[1] and Andrew Watson Sellards.

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One of the most prominent features of Asiatic cholera is the extremely rapid secretion of large amounts of fluid by the intestine during the early stages of the disease. The excretion of water by the ordinary channels practically ceases. The skin usually becomes dry and the urine is partially or completely suppressed. In cases of average severity this constant flow of fluid from the blood and other tissues into the intestines ceases only when there is no more available fluid in the body, and it usually recommences when liquid is supplied. This process might be regarded as a compensatory reaction for removing bacteria and their products and at the same time rendering conditions unfavorable for absorption from the intestine. Dangerous symptoms appear only when the supply of fluid fails, and these symptoms are relieved, at least temporarily, by the restoration of fluid to the body. Naturally, the restoration of fluid becomes an important matter and the various methods employed to accomplish this have attracted considerable attention. Sodium chloride is the solution which is in common use, and the concentrations employed usually have been divided under a physiologic classification into three groups, namely, (1) hypotonic, (2) isotonic, and (3) hypertonic solutions. The theoretical value of these three concentrations may briefly be outlined as follows: The hypotonic solution, by reason of its subnormal osmotic pressure, would tend to continue the excretion of water from the vascular system into the intestine, necessitating, perhaps, the frequent injection of relatively large amounts of salt solution. The hypertonic solution would tend to restore water to the body with a minimum loss of injected fluid. By reason of the higher osmotic pressure of the hypertonic solutions the loss of fluid from the blood vessels into the surrounding tissues might be delayed, thereby checking the diarrhœa. This increase of tonicity, if it were sufficiently pronounced, might even result in absorption of fluid from the intestine. This, of course, would be accompanied by the possibility of the absorption of bacterial products. However, in practice, it is not supposed that the solutions employed are sufficiently strong to cause any such harmful action. The effect of the isotonic solution would fall between these two extremes, and presumably it would not interfere with the natural processes of the body. The essential question is whether one should attempt to maintain the circulation with the use of as little fluid as practicable, checking the diarrhœa if possible, or whether liberal amounts of fluid should be used, allowing the diarrhœa to continue. In some respects the absolute cessation of excretion by all channels is less desirable than a limited amount of diarrhœa.

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Hypertonic salt solution has been in use for several years in the treatment of the stage of collapse in cholera, but Rogers recently has used it extensively and has reported very favorable results. He compared the results obtained with hypertonic solution of 1.3 per cent with those obtained with a hypotonic solution of 0.6 per cent.

In the autumn of 1909 a small epidemic of cholera occurred in Manila and at the request of Doctor Strong the effect of different concentrations of salt solution for treatment were again studied. Two solutions were tested, an isotonic one of 0.85 per cent and a hypertonic of 1.3 per cent. The first 10 cases in each series were treated with a Ringer's solution which was prepared according to the following formula: Sodium chloride, 0.8 per cent; potassium chloride, 0.04 per cent; and calcium chloride, 0.025 per cent for the isotonic and for the hypertonic solution, the sodium chloride was increased to 1.3 per cent, but the calcium and potassium salts were not changed. For the remaining cases sodium chloride only was used, in 0.85 per cent and 1.3 per cent solution.

In comparing different concentrations it is important, of course, to know the changes in the salt content of the blood. In the following work it has been assumed that the loss of salts occurred somewhat proportional to the loss of fluid and that the relative differences existing in the two salt solutions were not fundamentally altered after injection.

The cases were divided into two series as nearly comparable as possible. One of these series received isotonic and the other hypertonic salt solution. As a routine, 2 liters of fluid were injected intravenously in the course of one-half hour. The number and frequency of the injections was varied according to the individual case. In general, they were repeated when the pulse became weak and rapid and when the blood pressure registered between 50 and 70 millimeters of mercury.

Measurements of the blood pressure were made on all cases. Rising frequently from zero, the maximum was reached about one to three hours after the injection. This maximum varied somewhat in individual cases, but usually amounted to a slight rise above normal.

There was no apparent difference in the frequency with which the injections were required to be repeated in the two series of cases. The physical signs indicating the absorption of fluid by the tissues were quite similar after the use of either solution. Usually, after the second or third injection, the shrinking of the fingers disappeared, the skin over the extremities resumed its elasticity and the power of speech returned.

Neither the course of the diarrhœa nor the height of blood pressure which was obtained, bore any apparent relation to the solution which was employed. The following outline gives a general summary of the two groups.

Treatment.	Average number of injections.	Average maximum blood pressure after injections.	Deaths.						Total deaths.	Total recoveries.
			Collapse.				Uræmia.	Pneumonia.		
			First day.	Second day.	Third day.	Total.				
Isotonic	2	128	7	7	4	18	3	1	22	9
Hypertonic	1½	121	4	8	5	17	5	1	23	7

As regards the secretion of urine, no differences were observed. The proportion of cases dying in uræmia was practically unaffected by the use of the hypertonic salt solution. This agrees with Rogers' results.

In addition to the cases treated with hypertonic solutions of sodium chloride, a series of patients was treated in this hospital with hypertonic solutions containing relatively large amounts of sodium bicarbonate. This salt is of especial interest in the consideration of hypertonic solutions, since, in concentrated form, the bicarbonates have the property of withdrawing fluid from the tissues. Twelve cases admitted at the hospital received the alkaline hypertonic solution during the stage of collapse. The comparison of the three solutions in the treatment of collapse is as follows:

Solution employed.	Number of cases.	Death in collapse.	
		Number.	Per cent.
Neutral isotonic	31	18	58
Neutral hypertonic	30	17	57
Alkaline hypertonic	14	7	50

However, the effect of the alkaline solution is not merely a question of hypertonicity. In addition to its property of attracting fluid from the tissues, it also has diuretic properties. These characteristics may be of equal importance with the ionic concentration of the solution in the interpretation of the treatment of collapse. A detailed report of the series treated with alkali appears in the present number of the JOURNAL.

Records of the blood pressure were of interest in connection with the development of uræmia. In some cases, the blood pressure remained about normal during the stage of reaction, urine was excreted freely and recovery usually followed. However, in another class it rose rapidly during the stage of reaction, the excretion of urine was limited in amount or lacking altogether, and a fatal uræmia usually followed.

In severe cases which recovered, the urine frequently diminished in volume about one-half toward the end of the first week, or early in the second week of a normal convalescence. This fact is of considerable importance because of the prognostic value of the output of urine.

SUMMARY.

1. No definite differences for the two concentrations of salt solution which were tested for treatment, were observed, either upon the course of the disease or in its final termination.

2. Measurements of the blood pressure were of some service in determining the frequency with which repetitions of the injections of salt solution should be given.

In considering these results and conclusions, it is important to emphasize the severity of the cases under observation. The patients were often admitted to the hospital in complete collapse and, perhaps, were not particularly suited for such an investigation, since in many instances the beneficial effects following the usual treatment with ordinary salt solution were not obtained. Also, the total number of cases (61) was small and observations upon a larger series of patients under more favorable conditions might possibly give greater differences in the effect of the various concentrations of salt solution.

THE CHEMICAL COMPOSITION OF THE BLOOD IN ASIATIC CHOLERA.

By Hans Aron.

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All attempts to counteract the action of the toxins of the cholera vibrio, directly or indirectly, have thus far failed to give satisfactory results in the treatment of Asiatic cholera. There is at present only one method which is of distinct value in this disease, namely, the injection of large quantities of saline solution. Of course, this treatment is only symptomatic, tending to replace the great loss of water, but the curative action of its replacement is so great that without doubt we must regard loss of water as one of the main factors producing the grave results of the disease. The idea is a very old one that loss of fluid from the body is one of the most important factors in Asiatic cholera. The autopsy findings, such as a dry skin, peritoneal cavity and pericardial sac, as well as the increased viscosity of the blood, all confirm this belief. Investigators have repeatedly considered the question as to the effect of a great loss of fluid on the composition of the tissues of the body and of the extent to which changes in the composition of the tissues and fluids of the body are concerned in producing the stage of collapse and early death in Asiatic cholera. The earliest and most authoritative investigations of the chemical composition of the blood were made in 1850 by C. Schmidt[1] in Dorpat. However, Schmidt's conclusion that there is a constant withdrawal of water from the blood in stages of collapse has been doubted by several authors because he used too few control subjects. The following question also frequently has been discussed during recent years: Does the blood, in addition to the loss of water, also suffer a loss of salts, and, if so, to what degree? The answer is without doubt of great importance in the treatment of Asiatic cholera, since, if water alone is lost from the blood, then we need only to replace it; but if this is true of salts as well, then the latter must also be restored by the injection of an equivalent amount.

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[1] Zur Characteristik der epidemischen Cholera gegenüber verwandten Transsudationsanomalien. Leipzig, 1850.

Two years ago, Rogers[2] stated that there is not only a great loss of water in cholera, but, especially in severe cases, of the salts (chlorides) in proportionally greater amounts than water, the blood becoming hypotonic. Therefore, he suggested the injection of hypertonic saline solution and not of a normal solution such as is usually employed. In recent papers[3] he describes very favorable results by this method of treatment. As already mentioned, Rogers bases his treatment on the fact that he found a diminution of the chlorides in the blood. The accuracy of his chemical method of estimating the content of chlorides in the blood or blood serum is open to criticism; furthermore, his differences depend upon results showing that the blood of the average healthy Bengalese contains relatively more chlorides than that of Europeans.

I have undertaken a number of further analyses because of the important bearing which the composition of the blood in cholera may have upon the pathogenesis of the disease and its successful treatment, and I began with a number of cholera patients who were brought to the San Lazaro Hospital for Infectious Diseases.

Blood samples were taken from a vein in the arm of the patient before treatment had been instituted. It is often quite difficult and sometimes impossible, especially in the stage of severe collapse, to secure even a few drops of blood in this way. In addition to the above, material was not abundant this year because the incidence of the disease in the city of Manila was very small, only two or three cases occurring per day, and a number of these were children. All the patients from whom blood was taken showed the typical picture of cholera, and the clinical diagnosis in each instance was verified at the biological laboratory of the Bureau of Science by a bacteriologic examination of the fæces. It seemed better, as was done by Rogers, to estimate the chlorides as an index of the most important changes in the salt content of the blood, rather than to determine the total ash, because the latter course never gives such exact results.

Twenty or 30 cubic centimeters of the blood were poured into a glass-stoppered weighing-bottle filled with a mixture of oxalate solution and a few drops of formalin, the weight of these fluids having previously been determined. To be used for the determination of the total solids, a second sample of 2 to 5 cubic centimeters was at the same time put into a weighed, empty, glass-stoppered bottle. The two were then sent to the laboratory as quickly as possible, again weighed, and weighed portions of the samples taken for analysis. The content of chlorides alone was determined in the first sample, and, as a rule, two parallel analyses were made.

It was my intention to make the first determinations according to Neuman's method[4] which in former experiments has given very satisfactory results.

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[2] *This Journal, Sec. B* (1909), 4, 99.

[3] *Therap. Gaz.* (1909), 33, 761.

[4] *Ztschr. physiol. Chem.* (1903), 37, 115.

Not having the usual apparatus at hand, I improvised one, but the results were too low, either because the glass connection, ground by myself, was not absolutely tight, or the 1-liter bottle was too large. I therefore abandoned this method and mixed the blood with 2 or 3 grams of chemically pure sodium carbonate, dried it in a nickel dish and incinerated it at a very low temperature but only to the point when all organic material was destroyed, no effort being made to burn the charcoal. The incinerated material was extracted several times with hot water, the filtrate precipitated with silver nitrate, and the ash and filter then washed with dilute nitric acid. The extracts very often had a slightly yellow color. In these cases the following technique proved to be very satisfactory:

After precipitation with silver nitrate, the solution was boiled and a 5 per cent solution of potassium permanganate added, drop by drop, until a faint rose color appeared; the excess of potassium permanganate was then reduced by a few drops of ferro-ammonium-sulphate solution. The permanganate oxydized all the light yellow organic material, the fluid became clear, and at the same time the silver chloride became fully flocculent. The latter was determined gravimetrically in some cases, and one of the two samples was titrated by Volhard's method.

The water content of the blood was determined in the second sample by drying at 99° to 100° to a constant weight. Several samples of blood serum from cholera patients were also analyzed in the same way. Obviously, it is more difficult to secure a sufficient amount of serum than it is of blood, for analyses. For comparison, I analyzed blood and blood-serum of Filipino boys and students. I found practically the same composition as obtains with normal Europeans.

The second part of the study covered the examination of the blood of persons dead of cholera. While one would expect to find a pronounced change in the composition of the blood in cases which die and which therefore are the most severe, yet, so far as I could discover, no analyses heretofore have been made of the blood of cholera corpses. Through the courtesy of Dr. Vernon L. Andrews, of the department of pathology of the Philippine Medical School, I received blood samples from a number of Filipinos shortly after death, in whom the post-mortem findings and the bacteriologic examination of the fæces established the diagnosis of cholera. The blood was taken from the large veins of the heart before performing the autopsy and samples of from 200 to 250 cubic centimeters were secured without trouble. The results of my analyses are recorded in the following tables. I also append those of Schmidt and, for comparison, some recent ones of *normal blood.*

According to the analyses of Biernacki,[5] Erben,[6] and Dennstedt and Rumpf,[7] the following values can be regarded as the normal, average composition of human blood.

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[5] *Ztschr. klin. Med.* (1894), 24, 460.

[6] *Ibid.* (1900), 40, 266–293.

[7] *Ztschr. physiol. Chem.* (1904), 41, 42–54.

Composition of normal blood.

	Solids.	Chlorides.	Na_2O.	K_2O.	P_2O_5.
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*
Biernacki, Erben, and Dennstedt	19.7 to 22.8	0.26 to 0.28	0.16 to 0.19	0.14 to 0.18	About 0.08
Aron:					
Normal Filipino blood	21.3	0.265			0.085
Blood of M. Rosario who recovered from cholera	19.9	0.264			

Analyses of cholera blood (Schmidt).

No.	Sick.	Died.	Solids.	Chlorides.	P_2O_5.	K_2O.	Na_2O.	Phosphate of— Calcium.	Phosphate of— Magnesium.
			Per cent.	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*
VII	3 hours	18 hours	25.26	0.228	0.031	0.194	0.158	0.032	0.096
II	7 hours	Cured	23.91						
IV	9 hours	18 hours	25.47	0.222	0.075	0.203	0.150	0.046	0.047
VI	12 hours	10 hours	24.30	0.259	0.089	0.225	0.140	0.074	
V	18 hours	Cured	21.94	0.221	0.061	0.166	0.172		
III	36 hours	24 hours	23.90	0.195	0.081	0.184	0.111	0.086	
I	48 hours	3 days	21.38						
Normal			21.02	0.262	0.077	0.173	0.190	0.039	

Analyses of cholera serum (Schmidt).

	Solids. Per cent.	Chlorides. Per cent.
VII	13.83	0.354
II	12.01	....
VI	16.08	0.296
V	10.41	0.305
III	11.18	0.314
I	9.97	....

Analyses of blood of cholera patients (Aron).

No.	Name.	Stage of disease at time specimen was taken.	Chlorides, per 1,000.	Water.	Solids.	Remarks.
				Per ct.	*Per ct.*	
1	Basil. Pagad	Collapse, second day	2.13	-------	-------	
2	Primit. Agui	do	2.24	-------	-------	
3	Mar. Ablao	Collapse; 8 hours sick; recovered.	-------	77.1	22.9	
4	Alf. Catonj	do	-------	73.8	26.2	
5	Mar. Rosario	Collapse, first day; recovered.	2.27	71.8	28.2	Blood analyzed after recovery as "normal" blood.
6	Juan Tobias	Collapse, second day; died	2.31	73.5	26.5	
7	Kuada Diose	End of collapse; third day died.	2.30	71.5	28.5	
8	Eulal. Gonzal	Beginning uræmia	2.17	78.5	21.5	
9	Herb. Mercado	Uræmia fifth day: recovered.	2.25	78.5	21.5	
10	Eug. Mendoza	Uræmia sixth day; died	1.94	77.6	22.4	
-----	Maxim. Aorro	Died	2.45	-------	-------	Bacteriologically not cholera.

Analyses of serum of cholera patients (Aron).

Name.	Stage of disease.	Chlorides, per 1,000.	Water.	Solids.	Remarks.
			Per ct.	*Per ct.*	
Maximo Aorro	8 hours sick	3.44	87.6	12.4	Bacteriologically not cholera.
Maria Albao	8 hours sick; collapse	3.10	87.1	12.9	Died sixth day.
Ino. Villera	15 hours sick; collapse	3.15	85.8	14.2	Recovered.
Brig. Panjamban	Uræmia	2.58	87.7	12.3	Died seventh day.

Analyses of normal serum of Filipinos (Aron).

	Chlorides (per cent).	Water (per cent).	Solids (per cent).
Fi.	3.84	90.6	9.4
Ga.	3.64	90.4	9.6
Sa.	......	91.4	8.6

Analyses of cholera blood obtained at autopsy (Aron).

Name.	Solids.	Water.	Cholorides, per 1,000.	P_2O_5, per 1,000.	CaO, per 1,000.	K_2O, per 1,000.	Na_2O, per 1,000.	Protein N × 6¼.
	Per cent.	*Per cent.*						*Per cent.*
Dem. Esguerr	---------	---------	2.24	---------	---------	---------	---------	---------
A. del Ros	---------	---------	2.13	---------	---------	---------	---------	---------
Andr. Vent	27.6	72.4	---------	---------	---------	---------	---------	---------
Paul Romano	28.3	71.7	2.22	---------	---------	1.98	1.29	27.1
Euseb. Gonz	26.3	73.7	2.16	1.15	---------	---------	---------	25.9
Lor. Caccha	28.8	71.2	2.26	1.30	0.08	---------	---------	27.3
2 cases 1908	28.01 27.46	---------	---------	---------	---------	---------	---------	---------

All of the blood samples obtained at autopsy show a more or less decided decrease of water and a corresponding increase of solids. Taking about 20 per cent of solids as normal, the increase amounts to as much as 8.5 per cent.

The blood from cholera patients, in four cases, shows a decrease in the water content of the same degree as that found in the dead bodies, but four others had either a normal water content, or only a slight diminution. Therefore, it would be but natural to conclude that the blood is more highly concentrated in severe cases than in mild ones. Unfortunately, there is no accurate criterion of the severity of a given case, but if we assume that the patients who recover constitute the mild cases and those who die the severe ones, then there is not the slightest indication that the water content bears any relation to the severity of the disease. While the number of analyses I have made is too small to enable us to arrive at any final conclusion, I do not believe it will be possible to fix a constant relationship between the severity of the disease and the loss of water from the blood, because the interval of time during which the loss of water takes place must play an important rôle.

Another fact would seem to be of importance: The four cases with a low water content of the blood were in the early stages of the disease at the time the samples were taken, having been sick for from one to three days only. The figures for these cases agree well with the results obtained by Schmidt, for his patients also show an increase of solids in the blood in the early, but not in the later stages of cholera. The chloride content of the blood is decreased in nearly all instances investigated by myself as well as by Schmidt, a result which so far agrees fully with that of Rogers.

Is Rogers's conclusion that the blood has become hypotonic also correct? We have seen that the blood of cholera patients loses water. An *isotonic* blood, with a lower content of water, should have a lower content of salts (chlorides). The decrease in salts (chlorides) in itself does not prove that the blood has become *hypotonic*. The quantity of salts is often reduced in relation to the amount of total solids, but this calculation is apt to convey a wrong idea with regard to the tonicity of the fluid. The quantity of the salts should be compared in relation to the quantity of water and then it should be determined whether the loss in salts is proportional to the loss in water, or greater or less. If we do this, we will see that in the samples obtained during the first three days of the disease we can scarcely speak of a greater loss in the salts than would correspond to that of water. Of course, in the later stage of the disease, in Schmidt's analyses as well as in my own, the water content of the blood is almost normal, while that of salts, estimated as chlorides, is below that point. At this time, which corresponds to that of the uræmic stage of the disease, we really would have a hypotonic blood. It is worth noting that Rumpf[8] and Dennstedt also found a very great decrease in salts with but slight decrease in water in the blood of a man dying of nephritis (in uræmia).

The composition of the blood obtained at autopsy is exactly the same as that in the stage of collapse, during which all of these persons died. The water in almost all of these instances is decreased to 72 per cent. I found in this blood a marked decrease in the content of sodium, and a slight increase in that of potassium and of phosphorus. The results agree with those of the more extended analyses of Schmidt. This increase in potassium is readily explained if we consider that cholera blood contains a higher percentage of red blood cells than is normal. Schmidt pays special attention to the increase in phosphorus. While I found the same, I do not consider it at all remarkable, for the rise in the percentage of red blood cells and protein probably accounts for the higher phosphorus content of the blood.

The analyses of the sera also show a decrease of water and chlorides in cholera as compared with normal serum. The loss of the blood in water, as shown by these analyses as well as by those of Schmidt, is partly due to the loss of the serum in water, but the latter must also leave the red blood cells. The reduction of chlorides and water shown by the analyses of the serum confirms the observation made on samples of the entire blood.

SUMMARY.

In the stage of collapse in cholera a loss of water in the blood is regularly encountered, accompanied by a corresponding loss of chlorides (salts). This water loss is constantly high in the blood of persons who have died of cholera. In the later stages of the disease, the blood again shows an almost normal content of water, but the salts are not replaced to the normal amount. Therefore, the blood at this stage has a diminished salt content and is hypotonic.

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[8] *Münchener med. Wchnschr.* (1905), 52, 393.

CHOLERA AND CHOLERA-LIKE VIBRIOS ENCOUNTERED IN THE PHILIPPINES.

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This paper is presented with the idea of elucidating some questions which arose in connection with the routine examination for cholera vibrios in the stools from suspected cholera cases.

The primary questions in the study were: (1) Whether any "cholera-like" vibrios in the Philippines might agglutinate in a low dilution of a specific anticholera serum and thus lead to error in the ordinary routine agglutination tests performed for the purpose of ascertaining the presence of cholera vibrios in the stools of cholera suspects or "carriers;" (2) whether any cholera vibrios lose their morphology or agglutinability under any conditions, but especially in mixed cultures sent in from the provinces for diagnosis; (3) whether any vibrios of the *El Tor* type could be discovered in the Philippines. As the work progressed two other questions arose: (4) Whether any of the "cholera-like" vibrios which do not agglutinate with a specific anticholera serum can under any conditions be made to acquire such agglutinability; (5) whether Dieudonne's medium is satisfactory for the isolation of cholera vibrios from the stools, and if so, whether it can be used to differentiate "cholera-like" vibrios from true cholera vibrios. Finally, the question (6) as to whether the hog might act as a "cholera carrier" in the Philippines, was investigated.

The work is not completed, but owing to the departure of both of us from the Philippines it has seemed advisable to publish at the present time what has been accomplished in the study.

We selected for the work a series of vibrios isolated by various members of the staff and ourselves from specimens of fæces received at the laboratory during the summer and autumn of 1909 and first divided the organisms into two groups, cholera and noncholera vibrios, as differentiated by their reactions with a cholera serum of high potency.

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We have excluded from the "cholera-like" vibrios water vibrios which may be differentiated readily from the cholera organisms, and which have no right to be classified as "cholera-like" organisms; and retained in the class of noncholera vibrios those isolated from human intestinal contents or from water and which are indistinguishable from the cholera organisms except by the agglutination test, or by Pfeiffer's reaction.

TABLE I.—*Cholera and noncholera vibrios studied.*

CHOLERA VIBRIOS STUDIED.

No.	Name.	Date.	Origin.	Remarks
		1909.		
1	Regala I	May 27	Human intestine	Typical cholera, Pampanga.
2	Regala II	June 10	do	Do.
3	Salas	June 19	do	Do.
4	Miraflores	June 25	do	Do.
5	Nicolas	June 20	do	Do.
6	David	June 21	do	Do.
7	Bautista	July 10	do	1 typical cholera; first case in Manila, 1909.
8	Ramon	July 6	do	Typical cholera, Albay.
9	Sucero	July 9	do	Do.
10	C. Robles	Aug. 31	do	Typical cholera, Bulacan.
11	Dizon		do	Typical cholera, Manila.
12	Aniceto		do	Typical cholera, Pangasinan.
13	Maquio	Oct. 9	do	Typical cholera, Cavite.
14	Sucgang		do	Reported as infantile convulsions, Manila.
15	Calderon		do	Typical cholera, Manila.
16	Lorenzo		do	Do.
17	Cavite I		do	Do.
18	Cavite II		do	Do.
19	953		do	Do.
20	955		do	Do.
21	956		do	Do.
22	989		do	Do.
23	1029		do	Do.
24	1038		do	Do.
25	1041		do	Do.
26	1057		do	Do.
27	1101		do	Do.
28	1104		do	Do.
29	1108		do	Do.
30	1131		do	Do.
31	Camay	June 1	do	Typical cholera specimen received on agar after 15 days in transit from Mindanao.
32	Abalogan	July	do	Typical cholera specimen on agar, 7 days in transit from Samar.
33	Berezosa	July 7	do	Light case; specimen on agar 7 days in transit from Samar.
34	León	July 28	do	Typical case; dead in 5 hours, Manila.
35	Solitana		do	Typical case; specimen on agar 7 days in transit from Oriental Negros.

TABLE I.—*Cholera and noncholera vibrios studied*—Continued.

NONCHOLERA VIBRIOS STUDIED.

No.	Name.	Date.	Origin.	Remarks.
		1909.		
1	No. 135	Apr. 15	Human intestine.	Amœbic dysentery.
2	Iris	June ?	Water	Estero at Calle Iris.
3	Notbil	June 6	Human intestine.	Necropsy, pelvic peritonitis, salpingitis.
4	Gapus	Aug. 18	do	Post-mortem decomposition of all organs.
5	Sande	Sept. 8	do	Mild case of cholera. This vibrio found in addition to true cholera vibrios.
6	Sta. Monica	Sept. 11	Water	Stagnant pool which received human excretions.
7	Malabon	do	do	Specimen from water left in fishing boats after the fish had been unloaded.
8	Hagonoy	do	do	From water in bottom of boats after fish had been unloaded.
9	Orani	Oct. ?	do	From fishing boats.
10	Navotas A	Oct. 14	Clams	
11	Navotas B	do	do	
12	Navotas C	do	do	
13	Sandejas A		Water	Stagnant water which received house wastes, including human excrement.
14	Sandejas B		do	
15	Sandejas C		do	
16	Sandejas D		do	
17	Carolina		do	Large unprotected well without walls.
18	Bilibid		do	"Estero de Bilibid" which receives human excrement.
19	869		Human intestine.	
20	568		do	
21	371		do	
22	75		do	
23	48		do	
24	21		do	

Great difficulty was experienced formerly in securing bacteriological diagnoses of suspicious cases of cholera occurring in distant provinces. Often the examination of the specimens of fæces sent was futile. On the other hand, it was found that if ordinary alkaline agar slants were inoculated from the fæces and the cultures shipped in tin mailing cases cholera vibrios could frequently be isolated from such tubes even after they sometimes had been fifteen days in transit.

Two points should be accentuated in giving directions to health officers in distant places for the preparation of these cultures: (1) To place very little material on the slant; (2) to secure the specimen in the first twenty-four hours of the illness, if possible. When these directions are followed, the tubes often present isolated colonies of cholera vibrios upon arrival at the laboratory, and even if they do not appear so promising, recovery of the vibrios from them is often not difficult by the ordinary peptone and agar plate method.

We have found no media which would differentiate cholera from noncholera vibrios, although we have had an opportunity to test the elective blood-alkali-agar medium of Dieudonné (2) with fresh cholera material. *Cholera vibrios grow luxuriantly upon this medium, but other cholera-like vibrios also grow well.* However *Bacillus typhosus* does not develop on it and colon bacilli scarcely grow at all. Some other intestinal bacteria also flourish, but not luxuriantly, and less care is necessary in manipulation because many air-borne organisms either do not grow at all or develop so slowly as to be a negligible quantity. Tested side by side with ordinary agar plates, the relative number of cholera colonies is enormously increased, they develop faster, and, in favorable cases upon direct inoculation without preliminary enrichment in peptone, the diagnosis may be made therefrom in ten hours.[3]

Some of the noncholera vibrios which we examined did not differ more markedly from cholera vibrios in morphology, motility, cultural characteristics, production of cholera-red and pathogenicity, than may two individual cholera strains. They develop in peptone with the same rapidity and the colonies present the same appearance upon agar plates as do those of cholera vibrios.

Zlatogoroff, (12) in an interesting article, has called attention to the various characteristics of the cholera vibrio which have been relied upon for diagnosis and found wanting in the past, namely, growth upon gelatine, cholera-red production, absence of phosphorescence, absence of hæmolytic power, failure to produce a soluble toxin, and others. He admits the specificity of Pfeiffer's reaction, but is inclined to think that agglutinability is a quality which might be acquired and lost with surprising facility. He concluded that the life of cholera vibrios in water reduced their agglutinability, but that this quality could be restored by certain procedures.

Zlatogoroff worked with a total of 23 vibrios and a cholera serum with an agglutinating limit of 1–20,000. He found that 5 of these strains would agglutinate in a dilution of 1–5,000 and he at once considered them to be cholera vibrios. After one month he noticed that 3 of the others showed agglutination in a dilution of 1–500. These had been transplanted once a week and kept twenty-four hours in incubators at 37°C. and then at 16° to 18°C.

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[3] Doctor Bowman of the biological laboratory, Bureau of Science, has used this medium in the routine examination of 200 specimens sent by the Bureau of Health. The specimens were received as fæces, agar streak cultures, peptone cultures, portion of the intestine, etc. Streak cultures were made directly on the Dieudonné medium. When cholera was present the organism grew luxuriantly, overgrowing all others. A loop of the culture on the plates was transferred to a drop of agglutinating serum on a slide, and the diagnosis quickly made, while in using ordinary alkaline agar plates it was necessary sometimes to examine several colonies before a positive reaction was obtained. The use of this medium certainly simplifies the technique in the rapid bacteriologic diagnosis of cholera and at present it is being employed in the routine examination of all specimens sent to this laboratory.

He passed his organisms through animals (guinea pigs), once in three or four weeks, and after 54 generations raised the agglutinability so that it was exhibited in a dilution of 1-10,000. He was able to accomplish this only after he combined animal passage at rather infrequent intervals, with frequent transplanting upon good media. Neither of these methods alone sufficed to develop agglutinative properties. For example: Culture 15; dose ⅓ slant; November 6, no agglutination; November 6, ⅓ slant, guinea pig, died on November 9. Culture peritoneal on agar; November 10, agglutination 1-200; November 24, same repeated, agglutination 1-400; the same culture passed through 4 pigs without intermediate culture only developed an agglutinative power of 1-100.

He continued this treatment for three months, at the end of which time the vibrio had agglutinated in a dilution of 1-5,000. The culture transplanted without animal passage for three months agglutinated in 1-200.

To summarize his work, there were in all twenty-three vibrios studied: 5 agglutinated at the beginning in a dilution of 1-5,000; the agglutinating titre of the serum was 1-20,000; 18 vibrios did not agglutinate; 10 acquired agglutinative properties after six months, in a dilution of 1-5,000; 7 remained negative; and 1 died out.

Zlatogoroff concluded that during cholera epidemics, in addition to typical forms, atypical cholera vibrios which have lost certain biologic qualities may also be present in water. In time, under certain artificial conditions, these vibrios regain all the qualities of the typical cholera vibrios. He states: "Failure to agglutinate these water vibrios does not prove that they are not cholera, as cholera vibrios can change into saphropytic subvarieties very easily and can also lose their ability to agglutinate with cholera serum."

Barrenscheen (1) repeated that part of the work of Zlatogoroff which related to the reduction of agglutinability by keeping the vibrio for varying periods in water. He found that a cholera vibrio which agglutinated in a dilution of 1-40,000 at the beginning, did not agglutinate above 1-5,000 after eight days in distilled water. Cultures upon agar from the bacterial residue after centrifugation was also tested. The agglutinability had dropped to 1-400. Restoration or increase of agglutinability was not achieved after three weeks, although Barrenecheen succeeded in increasing the luxuriance of growth. He concludes that there is a passing out of the agglutinable substance into the water.

To test whether noncholera vibrios may acquire agglutinability to cholera serum, 12 of our own strains which seemed most favorable were selected. They all possessed a morphology, motility, and cholera-red production similar to those of cholera vibrios. They were treated in a manner similar to that suggested by Zlatogoroff. They were passed through guinea pigs between November 1 and 8, December and January, and transplanted upon agar every five or six days. After each animal passage, agglutination tests were made with a good cholera serum. At the end of two months, with 3 animal passages and 12 intermediate transplantations, not the slightest change was noticeable in the behavior of the organism to cholera agglutinating serum.

Our vibrios isolated from the human intestines, from water or other sources which are negative to agglutination tests with cholera serum and *classified by us as noncholera, do not develop agglutinability to cholera serum when treated as described by Zlatogoroff.*

The vibrios isolated by him from water and which "developed" agglutinability with cholera serum in a dilution of 1–10,000 must have been cholera vibrios.

For instance, his culture No. 15, cited above; with a dose of ⅛ slant, on November 6 showed no agglutination; ⅓ of a slant was injected into guinea pig. The guinea pig died on November 9. One transplant was made on November 10 and the agglutination was 1–200.

On the other hand, we have not been able at all to increase agglutinability.

Preparation of sera.—Sera were prepared with 10 cholera strains, 2 *El Tor* strains, and from 9 noncholera vibrios in the following manner: Eighteen-hour cultures on agar were used; suspensions were made with salt solution. Each rabbit received 4 or 5 injections; the interval between injections usually being seven to eight days. The amounts injected were as follows:

First day, 1 loop heated one hour at 60°C., into ear vein.
Eighth day, 3 loops heated one hour at 60°C., into ear vein.
Sixteenth day, 5 loops heated one hour at 60°C., into ear vein.
Twenty-fourth day, ½ slant, living, intraperitoneally.
Thirty-second to thirty-fourth day, 1 slant, living, intraperitoneally.
On the fortieth to forty-fourth day the animal was bled.

Selection of an animal for the preparation of a specific serum.—Kolle and Gotschlich (4) tested the normal sera of rabbit, ass, horse, goat and ox upon vibrios and found that normal rabbit and ass sera had a very slight agglutinating action upon vibrios, while horse and goat sera sometimes exert an agglutinating action in a dilution of 1–40 or 1–50. The small quantity of serum obtainable from a rabbit is usually considered a great disadvantage, but we found that large amounts of good serum could be obtained by the following procedure:

The bleeding apparatus consisted of an ordinary, large test tube with a rubber cork perforated to admit two glass tubes. A short piece of rubber tubing and a long slender needle is attached to one of these glass tubes; the other is connected with the vacuum pipe by about a meter of heavy rubber tubing. After sterilization, the needle is inserted below the ensiform cartilage and a trifle to the left, and then pushed upward into the pericardium and heart. After passing through the integument the needle in passing upward meets very slight resistance until the pulsating heart is encountered, but with a slight additional pressure it passes through the ventricular wall and blood begins to drip into the tube. The vacuum is turned on to facilitate the flow. In this way 10 to 15 cubic centimeters can be obtained without trouble at one bleeding.

Rabbits may be bled upon three successive days, the product of the three bleedings being combined and tested at the same time. In this way plenty of serum is available and the rabbits are apparently unharmed by the operation.

In 1895 the use of cholera agglutinin in the differential diagnosis between cholera and similar vibrios was recommended by Gruber and Durham (3) and at about the same time by Pfeiffer and Kolle (9).

The relation of nonspecific vibrios which resembled cholera, to the latter was clearly defined and the absolute specificity of the cholera vibrio demonstrated by the work of Kolle and Gotschlich (4).

They found that many vibrios existed which morphologically and biologically were indistinguishable from the real cholera organism, except by the use of a specific cholera serum. Such a specific cholera serum which agglutinated cholera organisms in a dilution of 1-5,000 or 1–10,000 had no more effect upon noncholera vibrios than normal serum from the same species of animal and sera prepared from noncholera vibrios had as little effect upon cholera vibrios.

Strong agglutinating cholera serum, in consequence of its richness in cholera agglutinin in dilutions of 1–2,000, 1–3,000, 1–5,000, serves for differentiating cholera from nonspecific vibrios. Kolle remarks that differences in the agglutinability of individual cholera strains make little difference, as the strains most refractory to this reaction will show positive results in an hour.

Kolle and his co-workers were unable to produce a serum with the noncholera vibrios which had any more effect upon genuine cholera vibrios than normal rabbit serum. He noted a great variation among the individual cholera strains in morphology, motility, cholera-red production, pathogenicity and cultural characteristics, and pointed out the unreliability of any or all of these characteristics and the absolute necessity of employing the agglutination test before making a diagnosis. With the exception of the old laboratory strains of Pfeiffer and Hankin, which seemed to be extremely susceptible to all agglutinating cholera sera, Kolle's cholera sera agglutinated the majority of cholera strains in a dilution 1–2,000 to 1–5,000, occasionally in higher dilutions, but in no instance did a cholera strain fail to agglutinate in a dilution of at least 1 to 1,000.

TABLE II.—*Agglutination tests.*

Name of culture.	Salt control.	Normal rabbit serum.			Serum Regala II.							
		1–10.	1–20.	1–50.	1–10.	1–20.	1–50.	1–100.	1–200.	1–500.	1–1,000.	1–2,000.
Regala I	—	—	------	------	+	+	+	+	+	+	+	+
Regala II	—	—	------	------	+	+	+	+	+	+	+	+
Salas	—	—	------	------	+	+	+	+	+	+	+	+
Miraflores	—	+	—	—	+	+	+	+	+	+	+	+
Nicolas	—	—	------	------	+	+	+	+	+	+	+	+
David	—	+	—	—	+	+	+	+	+	+	+	+
Bautista	—	------	------	------	+	+	+	+	+	+	+	+
Ramon	—	±	—	—	+	+	+	+	+	+	+	+
Sucero	—	—	------	------	+	+	+	+	+	+	+	+
C. Robles	—	—	------	------	+	+	+	+	+	+	+	+
Dizon	—	—	------	------	+	+	+	+	+	+	+	+
Anicete	—	—	------	------	+	+	+	+	+	+	+	+
Maquio	—	—	------	------	+	+	+	+	+	+	+	+

TABLE II.—*Agglutination tests*—Continued.

Name of culture.	Salt control.	Normal rabbit serum.			Serum Regala II.							
		1-10.	1-20.	1-50.	1-10.	1-20.	1-50.	1-100.	1-200.	1-500.	1-1,000.	1-2,000.
Sucgang	—	—	------	------	+	+	+	+	+	+	+	+
Calderon	—	—	------	------	+	+	+	+	+	+	+	+
Lorenzo S.	—	—	------	------	+	+	+	+	+	+	+	+
Cavite I	—	—	------	------	+	+	+	+	+	+	+	+
Cavite II	—	—	------	------	+	+	+	+	+	+	+	+
953	—	—	------	------	+	+	+	+	+	+	+	+
955	—	—	------	------	+	+	+	+	+	+	+	+
956	—	—	------	------	+	+	+	+	+	+	+	+
989	—	—	------	------	+	+	+	+	+	+	+	+
1029	—	—	------	------	+	+	+	+	+	+	+	+
1038	—	—	------	------	+	+	+	+	+	+	+	+
1041	—	—	------	------	+	+	+	+	+	+	+	+
1057	—	—	------	------	+	+	+	+	+	+	+	+
1101	—	—	------	------	+	+	+	+	+	+	+	+
1104	—	—	------	------	+	+	+	+	+	+	+	+
1108	—	—	------	------	+	+	+	+	+	+	+	+
1131	—	—	------	------	+	+	+	+	+	+	+	+
Camay	—	—	------	------	+	+	+	+	+	—	—	—
Abologan	—	—	------	------	+	+	+	+	±	—	—	------
Berezosa	—	—	------	------	+	+	+	+	±	—	—	------
Leon	—	—	------	------	+	+	+	+	±	—	—	------
Soletana	—	—	------	------	+	+	+	+	±	—	—	------
135	—	+	—	------	+	—	—	------	------	------	------	------
Gapus	—	------	------	------	—	—	—	------	------	------	------	------
Notbil	—	+	±	------	+	—	—	------	------	------	------	------
Sande	—	+	±	------	[illegible]	—	—	------	------	------	------	------
Santa Monica	—	—	—	------	—	—	—	------	------	------	------	------
Malabon	—	+	—	------	+	—	—	------	------	------	------	------
Hagonoy	—	+	—	------	—	—	—	------	------	------	------	------
Orani	—	—	------	------	—	—	—	------	------	------	------	------
Navotas A	—	—	------	------	—	—	—	------	------	------	------	------
Navotas B	—	—	------	------	—	—	—	------	------	------	------	------
Navotas C	—	—	------	------	—	—	—	------	------	------	------	------
Sandejas A	—	+	—	------	+	—	—	------	------	------	------	------
Sandejas B	—	—	------	------	—	—	—	------	------	------	------	------
Sandejas C	—	—	------	------	—	—	—	------	------	------	------	------
Sandejas D	—	—	------	------	—	—	—	------	------	------	------	------
Carolina	—	+	—	------	—	—	—	------	------	------	------	------
Bilibid	—	—	------	------	—	—	—	------	------	------	------	------
869	—	—	------	------	—	—	—	------	------	------	------	------
568	—	—	------	------	—	—	—	------	------	------	------	------
371	—	—	------	------	—	—	—	------	------	------	------	------
75	—	—	------	------	—	—	—	------	------	------	------	------
48	—	—	------	------	—	—	—	------	------	------	------	------
21	—	—	------	------	—	—	—	------	------	------	------	------
Iris	—	—	------	------	—	—	—	------	------	------	------	------

TABLE II.—*Agglutination tests*—Continued.

Culture.	Serum B. Robles.											
	1-10.	1-20.	1-50.	1-100.	1-200.	1-300.	1-400.	1-500.	1-1,000.	1-2,000.	1-4,000.	1-8,000.
Abalogan	+	+	+	+	+	+	+	+	+	—		
Berezosa	+	+	+	+	+	+	+	+	±	—		
Leon	+	+	+	+	+	+	+	+	±	—		
Solitana	+	+	+	+	+	+	+	+	±	—		
Ramon	+	+	+	+	+	+	+	+	+	+	+	+
Sucero	+	+	+	+	+	+	+	+	+	+	+	+
C. Robles	+	+	+	+	+	+	+	+	+	+	+	±
Dizon	+	+	+	+	+	+	+	+	+	+	+	+
Anicete	+	+	+	+	+	+	+	+	+	+	+	±
Maquio	+	+	+	+	+	+	+	+	+	+	+	±
Sucgang	+	+	+	+	+	+	+	+	+	+	+	±
Calderon	+	+	+	+	+	+	+	+	+	+	+	±
Iris	—											
Notbil	—											
Sta. Monica	—											
Sande	—											
Malabon	+	+	+	—								
Hagonoy	—											
Orani	—											
Navotas A	—											
Navotas B	—											
Sandejas A		±	—	—								
Sandejas B		tr.	—	—								
Gapus	—											
Bilibid	—											
B. Robles	+	+	+	+	+	+	+	+	+	+	+	±
King A	+	+	+	+	+	+	+	+	+	+	+	±
King B	+	+	+	+	+	+	+	+	+	+	+	±
869	—											
568	—											
371	—											
75	—											
48	+	tr.	—	—								
21	—	—										

TABLE II.—*Agglutination tests*—Continued.

Culture.	Serum King A.										
	1-10.	1-20.	1-50.	1-100.	1-200.	1-300.	1-400.	1-500.	1-1,000.	1-2,000.	1-4,000.
Abalogan	+	+	+	+	±	+	+	±	—	—	------
Berezona	+	+	+	+	±	+	+	±	—	—	------
Leon	+	+	+	+	+	±	+	±	—	—	------
Soletana	+	+	+	+	±	+	+	±	—	—	------
Ramon	+	+	+	+	+	+	+	+	+	+	±
Sucero	+	+	+	+	+	+	+	+	+	+	±
C. Robles	+	+	+	+	+	+	+	+	+	+	±
Dizon	+	+	+	+	+	+	+	+	+	+	±
Anicete	+	+	+	+	+	+	+	+	+	+	±
Maquio	+	+	+	+	+	+	+	+	+	+	±
Suegana	+	+	+	+	+	+	+	+	+	+	±
Calderon	+	+	+	+	+	+	+	+	+	+	+
Iris	—	—	—	------	------	------	------	------	------	------	------
Notbil	—	—	—	------	------	------	------	------	------	------	------
Sta. Monica	—	—	—	------	------	------	------	------	------	------	------
Sande	—	—	—	------	------	------	------	------	------	------	------
Malabon	—	—	—	------	------	------	------	------	------	------	------
Hagonoy	—	—	—	------	------	------	------	------	------	------	------
Orani	—	—	—	------	------	------	------	------	------	------	------
Navotas A	—	—	—	------	------	------	------	------	------	------	------
Navotas B	—	—	—	------	------	------	------	------	------	------	------
Sandejas A	—	—	—	------	------	------	------	------	------	------	------
Sandejas B	—	—	—	------	------	------	------	------	------	------	------
Bilibid	—	—	—	------	------	------	------	------	------	------	------
Gapus	—	—	—	------	------	------	------	------	------	------	------
King A	+	+	+	+	+	+	+	+	+	+	+
King B	+	+	+	+	+	+	+	+	+	+	±
869	—	—	—	------	------	------	------	------	------	------	------
568	—	—	—	------	------	------	------	------	------	------	------
371	—	—	—	------	------	------	------	------	------	------	------
75	—	—	—	------	------	------	------	------	------	------	------
48	—	—	—	------	------	------	------	------	------	------	------
21	—	—	—	------	------	------	------	------	------	------	------

TABLE II.—*Agglutination tests*—Continued.

Culture.	Serum Abalogan.								
	1–10.	1–20.	1–50.	1–100.	1–200.	1–500.	1–1,000.	1–2,000.	1–4,000.
Abalogan	+	+	+	+	+	+	+	±	—
Berezosa	+	+	+	+	+	+	+	±	—
Leon	+	+	+	+	+	+	+	±	—
Soletana	+	+	+	+	+	+	+	±	—
Ramon	+	+	+	+	+	+	+	±	—
Lucero	+	+	+	+	+	+	±	—	—
C. Robles	+	+	+	+	+	+	±	—	—
Dizon	+	+	+	+	+	+	±	—	—
Anicete	+	+	+	+	+	+	±	—	—
Maquio	+	+	+	+	+	+	±	—	—
Sucgana	+	+	+	+	+	+	+	±	—
Calderon	+	+	+	+	+	+	+	±	—
135	+	+	+	+	+	—	—	—	—
Iris	—	—	—	—	—	—	—	—	—
Notbil	tr.	—	—	—	—	—	—	—	—
Sta. Monica	tr.	—	—	—	—	—	—	—	—
Sande	tr.	—	—	—	—	—	—	—	—
Malabon	+	±	—	—	—	—	—	—	—
Hagonoy	±	—	—	—	—	—	—	—	—
Navotas A	+	±	—	—	—	—	—	—	—
Navotas B	±	—	—	—	—	—	—	—	—
Sandejas A	+	+	±	—	—	—	—	—	—
Sandejas B	+	+	±	—	—	—	—	—	—
Bilibid	—	—	—	—	—	—	—	—	—
Gapus	—	—	—	—	—	—	—	—	—
Orani	—	—	—	—	—	—	—	—	—
King A	+	+	+	+	+	+	+	+	—
King B	+	+	+	+	+	+	+	+	—
869	—	—	—	—	—	—	—	—	—
568	—	—	—	—	—	—	—	—	—
871	—	—	—	—	—	—	—	—	—
75	—	—	—	—	—	—	—	—	—
48	—	—	—	—	—	—	—	—	—
21	—	—	—	—	—	—	—	—	—
Carolina	—	—	—	—	—	—	—	—	—

TABLE II.—*Agglutination tests*—Continued.

Culture.	Salt.	Normal serum.		Serum Berezosa.								
		1-10.	1-20.	1-10.	1-20.	1-50.	1-100.	1-200.	1-400.	1-500.	1-1,000.	1-2,000.
Abalogan	—	—	------	+	+	+	+	+	+	+	+	+
Berezosa	—	—	------	+	+	+	+	+	+	+	+	±
Leon	—	—	------	+	+	+	+	+	+	+	+	±
Soletana	—	—	------	+	+	+	+	+	+	+	+	—
Ramon	—	—	------	+	+	+	+	+	+	+	+	------
Lucero	—	—	------	------	------	------	+	+	+	+	+	------
C. Robles	—	—	------	------	------	------	+	+	+	+	+	------
Dizon	—	—	------	------	------	------	+	+	+	+	+	------
Anicete	—	—	------	------	------	------	+	+	+	+	+	------
Maquio	—	—	------	------	------	------	+	+	+	+	+	------
Sucgana	—	—	------	------	------	------	+	+	+	+	+	------
Calderon	—	—	------	------	------	------	+	+	+	+	+	------
135	—	+	—	—	—	—	—	------	------	------	------	------
Iris	—	—	------	—	—	—	------	------	------	------	------	------
Notbil	—	—	------	—	—	—	------	------	------	------	------	------
Sta. Monica	—	—	------	—	—	—	------	------	------	------	------	------
Sande	—	—	------	—	—	—	------	------	------	------	------	------
Malabon	—	+	—	+	+	+	—	------	------	------	------	------
Hagonoy	—	—	------	—	—	------	------	------	------	------	------	------
Navotas A	—	—	------	—	—	------	------	------	------	------	------	------
Navotas B	—	—	------	—	—	------	------	------	------	------	------	------
Sandejas A	—	—	------	+	±	------	------	------	------	------	------	------
Sandejas B	—	—	------	+	±	------	------	------	------	------	------	------
Bilibid	—	—	------	—	—	------	------	------	------	------	------	------
Carolina	—	—	------	—	------	------	------	------	------	------	------	------
King A	—	—	------	+	+	+	+	+	+	+	+	------
King B	—	—	------	+	+	+	+	+	+	+	+	------
869	—	—	------	—	—	------	------	------	------	------	------	------
568	—	—	------	—	—	------	------	------	------	------	------	------
371	—	—	------	—	—	------	------	------	------	------	------	------
75	—	—	------	—	—	------	------	------	------	------	------	------
48	—	—	------	—	—	------	------	------	------	------	------	------
21	—	—	------	—	—	------	------	------	------	------	------	------
Gapus	—	—	------	—	—	------	------	------	------	------	------	------
Orani	—	—	------	—	—	------	------	------	------	------	------	------

TABLE II.—*Agglutination tests*—Continued.

Culture.	Salt.	Normal serum.			Serum Leon.								
		1-10.	1-20.	1-50.	1-10.	1-20.	1-50.	1-100.	1-200.	1-400.	1-500.	1-1,000.	1-2,000.
Abalogan	−	−	------	------	+	+	+	+	+	+	+	+	±
Berezosa	−	−	------	------	+	+	+	+	+	+	+	+	±
Leon	−	−	------	------	+	+	+	+	+	+	+	−	±
Soletana	−	−	------	------	+	+	+	+	+	+	+	+	±
Ramon	−	−	------	------	+	+	+	+	+	+	+	+	±
Lucero	−	−	------	------	+	+	+	+	+	+	+	+	+
C. Robles	−	−	------	------	+	+	+	+	+	+	+	+	±
Dizon	−	−	------	------	+	+	+	+	+	+	+	+	±
Anicete	−	−	------	------	+	+	+	+	+	+	+	+	------
Maquio	−	−	------	------	+	+	+	+	+	+	+	+	------
Suegana	−	−	------	------	+	+	+	+	+	+	+	+	∓
Calderon	−	−	------	------	+	+	+	+	+	+	+	+	+
135	−	−	------	------	−	−	−	------	------	------	------	------	------
Iris	−	−	------	------	−	−	−	------	------	------	------	------	------
Notbil	−	−	−	−	±	−	−	------	------	------	------	------	------
Sta. Monica	−	−	------	------	−	−	−	------	------	------	------	------	------
Sande	−	−	------	------	±	−	−	------	------	------	------	------	------
Malabon	−	±	−	−	∓	±	−	------	------	------	------	------	------
Hagonoy	−	−	−	------	−	−	−	------	------	------	------	------	------
Orani	−	−	------	------	−	−	−	------	------	------	------	------	------
Navotas A	−	−	------	------	−	−	−	------	------	------	------	------	------
Navotas B	−	−	------	------	−	−	−	------	------	------	------	------	------
Gapus	−	−	------	------	−	−	−	------	------	------	------	------	------
Sandejas A	−	−	------	------	±	±	−	−	------	------	------	------	------
Sandejas B	−	−	------	------	±	−	−	------	------	------	------	------	------
Carolina	−	−	------	------	−	−	−	------	------	------	------	------	------
Bilibid	−	−	------	------	−	−	−	------	------	------	------	------	------
King A	−	−	------	------	+	+	+	+	+	+	+	+	±
King B	−	−	------	------	+	+	+	+	+	+	+	+	±
B. Robles	------	------	------	------	------	------	------	------	------	------	------	------	------
869	−	−	------	------	−	−	−	------	------	------	------	------	------
568	−	−	------	------	−	−	−	------	------	------	------	------	------
371	−	−	------	------	−	−	−	------	------	------	------	------	------
75	−	−	------	------	−	−	−	------	------	------	------	------	------
48	------	------	------	------	------	------	------	------	------	------	------	------	------
21	−	−	------	------	−	−	−	------	------	------	------	------	------
Regala II	−	−	------	------	+	+	+	+	+	+	+	+	±

TABLE II.—*Agglutination tests*—Continued.

Culture.	Serum Soletana.										
	1–10.	1–20.	1–50.	1–100.	1–200.	1–300.	1–400.	1–500.	1–800.	1–1,000.	1–2,000.
Abalogan	+	+	+	+	+	+	+	+	±	—	
Berezosa	+	+	+	+	+	+	+	+	±	—	
Leon	+	+	+	+	+	+	+	+	+	+	—
Soletana	+	+	+	+	+	+	+	+	+	—	—
Ramon	+	+	+	+	+	+	+	+	+	+	—
Lucero	+	+	+	+	+	+	+	+	+	±	—
C. Robles	+	+	+	+	+	+	+	+	+	+	—
Dizon	+	+	+	+	+	+	+	+	+	—	—
Anicete	+	+	+	+	+	+	+	+	+	±	—
Maquio	+	+	+	+	+	+	+	+	±	—	—
Sucgana	+	+	+	+	+	+	+	+	+	+	—
Calderon	+	+	+	+	+	+	+	+	+	+	—
135	—	—	—	—							
Iris	—	—									
Notbil	—	—									
Sta. Monica	—	—									
Sande	—	—									
Malabon	+	+	±	—							
Hagonoy	—	—									
Orani	—	—									
Navotas A	—	—									
Navotas B	—	—									
Sandejas A	+	—	—								
Sandejas B	+	—	—								
Bilibid	—	—									
Gapus	—	—									
Carolina	—	—									
King A	+	+	+	+	+	+	+	+	+	±	
King B	+	+	+	+	+	+	+	+	+		
869	—	—									
568	—	—									
371	—	—									
75	—	—									
48	—	—									
21	—	—									

TABLE II.—*Agglutination tests*—Continued.

Culture.	Salt solution.	Normal rabbit serum, 1-10.	Serum King B.						
			1-40.	1-80.	1-100.	1-500.	1-1,000.	1-1,500.	1-2,000.
Abalogan	—	—	+	+	+	+	+	±	—
Berezosa	—	—	+	+	+	+	+	±	—
Leon	—	—	+	+	+	+	+	±	—
Soletana	—	—	+	+	+	+	+	±	—
Ramon	—	—	+	+	+	+	+	±	—
Sucero	—	—	+	+	+	+	+	±	—
G. Robles	—	—	+	+	+	+	+	±	—
Dizon	—	—	+	+	+	+	+	±	—
Aniceta	—	—	+	+	+	+	±	—	—
Maquio	—	—	+	+	+	+	±	—	—
Sucgang	—	—	+	+	+	+	+	±	—
Calderon	—	—	+	+	+	+	+	±	—
King A	—	—	+	+	+	+	+	±	—
King B	—	—	+	+	+	+	+	±	—
869			—						
568			—						
75			—						
48			—						
371			—						
Iris			—						
Notbil			—						
Sta. Monica			—						
Sande			—						
Sandejas A			—						
Sandejas B			—						
Gapus			—						

Culture.	Salt solution.	Normal rabbit serum 1-10.	Serum No. 2.					
			1-400.	1-500.	1-800.	1-1,000.	1-1,500.	1-2,000.
Abalogan	—	—	+	+	+	+	+	±
Berezosa	—	—	+	+	+	+	+	tr.
Leon	—	—	+	+	+	+	+	±
Solitana	—	—	+	+	+	+	tr.	—
2	—	—	+	+	+	+	+	±
4	—	—	+	+	+	+	+	±
5	—	—	+	+	+	+	+	±
6	—	—	+	+	+	+	+	±

TABLE II.—*Agglutination tests*—Continued.

Culture.	Serum No. 4.					
	1-400.	1-800.	1-1,000.	1-1,500.	1-2,000.	1-4,000.
Abalogan	+	+	+	+	+	—
Berezosa	+	+	+	+	±	
Leon	+	+	+	+	±	tr
Solitana	+	+	+	±	—	—
2	+	+	+	+	+	±
4	+	+	+	+	+	±
5	+	+	+	+	+	±
6	+	+	+	+	+	±

Culture.	Salt solution.	Normal rabbit serum, 1-10.	Serum No. 5.			
			1-500.	1-1,000.	1-1,500.	1-2,000.
Abalogan	—	—	+	+	±	—
Berezosa	—	—	+	+	±	—
Leon	—	—	+	+	±	—
Solitana	—	—	+	tr.	—	—
2	—	—	+	+	±	—
4	—	—	+	+	±	—
5	—	—	+	+	±	—
6	—	—	+	+	±	—

Culture.	Serum No. 6.					
	1-400.	1-800.	1-1,000.	1-1,200.	1-1,600.	1-2,000.
Abalogan	+	+	tr.	—	—	—
Berezosa	+	+	tr.	—	—	—
Leon	+	±	—	—	—	—
Solitana	+	+	tr.	—	—	—
2	+	+	+	+	±	tr.
4	+	+	+	+	±	tr.
5	+	+	+	+	±	tr.
6	+	+	+	+	±	tr.

TABLE II.—*Agglutination tests*—Continued.

Culture.	Serum Sandejas A.									
	1-10.	1-20.	1-50.	1-100.	1-200.	1-500.	1-1,000.	1-2,000.	1-4,000.	1-8,000.
Abalogan	—	—	—	------	------	------	------	------	------	------
Berezosa	—	—	—	------	------	------	------	------	------	------
Leon	—	—	—	------	------	------	------	------	------	------
Solitana	—	—	—	------	------	------	------	------	------	------
Ramon	—	—	—	------	------	------	------	------	------	------
Lucero	tr.	—	—	------	------	------	------	------	------	------
C. Robles	tr.	—	—	------	------	------	------	------	------	------
Dizon	tr.	—	—	------	------	------	------	------	------	------
Anicete	tr.	—	—	------	------	------	------	------	------	------
Maquio	+	—	—	------	------	------	------	------	------	------
Sucgana	tr.	—	—	------	------	------	------	------	------	------
Calderon	+	—	—	------	------	------	------	------	------	------
135	—	—	—	------	------	------	------	------	------	------
Iris	+	—	—	------	------	------	------	------	------	------
Notbil	+	—	—	------	------	------	------	------	------	------
Sta. Monica	—	—	—	------	------	------	------	------	------	------
Sande	—	—	—	------	------	------	------	------	------	------
Malabon	+	—	—	------	------	------	------	------	------	------
Hagonoy	—	—	—	------	------	------	------	------	------	------
Orani	—	—	—	------	------	------	------	------	------	------
Gapus	—	—	—	------	------	------	------	------	------	------
Navotas A	—	—	—	------	------	------	------	------	------	------
Navotas B	—	—	—	------	------	------	------	------	------	------
Sandejas A	+	+	+	+	+	+	+	+	+	±
Sandejas B	+	+	+	+	+	+	+	+	+	±
Carolina	—	—	—	------	------	------	------	------	------	------
Bilibid	—	—	—	------	------	------	------	------	------	------
B. Robles	—	—	—	------	------	------	------	------	------	------
King A	—	—	—	------	------	------	------	------	------	------
King B	—	—	—	------	------	------	------	------	------	------
869	—	—	—	------	------	------	------	------	------	------
568	—	—	—	------	------	------	------	------	------	------
371	—	—	—	------	------	------	------	------	------	------
75	—	—	—	------	------	------	------	------	------	------
48	+	+	+	+	+	+	+	+	+	±
21	—	—	—	------	------	------	------	------	------	------

TABLE II.—*Agglutination tests*—Continued.

Culture.	Serum Sandejas B.					
	1-50.	1-100.	1-200.	1-500.	1-1,000.	1-2,000.
Abalogan	—	—				
Berezosa	—	—				
Leon	tr	—				
Solitana	—	—				
Ramon	tr	—				
Lucero	tr	—				
C. Robles	tr	—				
Dizon	tr	—				
Anicete	tr	—				
Maquio	tr	—				
Sucgana	tr	—				
Calderon	tr	—				
135	tr	—				
Iris	—	—	—			
Notbil	—	—				
Sande	—	—				
Sta. Monica	tr	—				
Malabon	tr	—				
Hagonoy	—	—	—			
Orani	—	—	—			
Nabotas A	—	—	—			
Nabotas B	—	—	—			
Gapus	—	—	—			
Sandejas A	+	+	+	+	+	±
Sandejas B	+	+	+	+	+	±
Carolina	—	—	—			
Bilibid	—	—	—			
King A	—	—	—			
King B	—	—	—			
B. Robles	—	—	—			
869	—	—	—			
568	—	—	—			
371	—	—	—			
75	—	—	—			
48	+	+	+	+	+	±
21	—	—	—			

Table II.—*Agglutination tests*—Continued.

Culture.	Serum Navotas B.							
	1-20.	1-50.	1-100.	1-200.	1-500.	1-1,000.	1-2,000.	1-4,000.
Abalogan	—	—	—					
Berezosa	—	—	—					
Leon	±	—	—					
Solitana	—	—	—					
Ramon	±	—	—					
Lucero	±	—	—					
C. Robles	±	—	—					
Dizon	tr	—	—					
Anicete	tr	—	—					
Maquio	tr	—	—					
Sucgana	±	—	—					
Calderon	tr	—	—					
135	—	—	—					
Iris	—	—	—					
Notbil	—	—	—					
Sta. Monica	—	—	—					
Sande	—	—	—					
Malabon	+	+	—					
Hagonoy	—	—	—					
Orani	—	—	—					
Navotas A	+	+	+	+	+	+	+	±
Navotas B	+	+	+	+	+	+	+	±
Gapus	—	—	—					
Sandejas A	+	±	—	—				
Sandejas B	+	+	tr	—				
Carolina	—	—	—					
Bilibid	—	—	—					
King A	±	—	—					
King B	—	—	—					
B. Robles	—	—	—					
869	—	—	—					
568	—	—	—					
371	—	—	—					
75	—	—	—					
48	+	—	—					
21	—	—	—					

TABLE II.—*Agglutination tests*—Continued.

Culture.	Salt solution.	Normal rabbit serum, 1-10.	Serum No. 869.					
			1-50.	1-100.	1-200.	1-500.	1-1,000.	
Abalogan	—	—	—	—				
Berezosa	—	—	—	—				
Leon	—	—	—	—				
Soletana	—	—	—	—				
Ramon	—	—	—	—				
Sucero	—	—	—	—				
G. Robles	—	—	—	—				
Dizon	—	—	—	—				
Anicete	—	—	—	—				
Maquio	—	—	—	—				
Sucgang	—	—	—	—				
Calderon	—	—	—	—				
King A	—	—	—	—				
King B	—	—	—	—				
869	—	—	+	+	+	+	+	+
568			—	—				
75			—	—				
48			—	—				
371			—	—				
Iris			—	—				
Notbil			—	—				
Sta. Monica			—	—				
Sande			—	—				
Sandejas A			—	—				
Sandejas B			—	—				
Gapus			—	—				

TABLE II.—*Agglutination tests*—Continued.

Culture.	Serum No. 568.								
	1–20.	1–50.	1–100.	1–200.	1–500.	1–1,000.	1–2,000.	1–4,000.	1–8,000.
Abalogan	—	—	—						
Berezosa	—	—	—						
Leon	—	—	—						
Solitana	—	—	—						
Ramon	—	—	—						
Lucero	—	—	—						
C. Robles	—	—	—						
Dizon	—	—	—						
Anicete	—	—	—						
Maquio	—	—	—						
Sucgana	—	—	—						
Calderon	—	—	—						
135	—	—	—						
Iris	—	—	—						
Notbil	—	—	—						
Sta. Monica	—	—	—						
Sande	—	—	—						
Malabon	+	±	—						
Hagonoy	+	—	—						
Navotas A	tr	—	—						
Navotas B	—	—	—						
Sandejas A	+	—	—						
Sandejas B	+	—	—						
Bilibid	—	—	—						
Gapus	+	+	+	+	+	+	+	+	±
Orani	—	—	—						
B. Robles									
King A	+	±	—	—					
King B	+	±	—	—					
869	—	—	—						
568	+	+	+	+	+	+	+	+	—
371	—	—	—						
75	—	—	—						
48	+	—	—						
21	—	—	—						

TABLE II.—*Agglutination tests*—Continued.

Culture.	Serum No. 48.						
	1-50.	1-100.	1-200.	1-500.	1-1,000.	1-2,000.	1-4,000.
Abalogan	—	—					
Berezosa	—	—					
Leon		—					
Solitana	—	—					
Ramon		—					
Sucero		—					
C. Robles		—					
Dizon		—					
Anicete		—					
Maquio		—					
Suegang		—					
Calderon		—					
135		—					
Iris	—	—	—				
Notbil	—	—					
Sande	—	—					
Sta. Monica		—					
Hagonoy	—	—	—				
Orani	—	—	—				
Navotas A	—	—	—				
Navotas B	—	—	—				
Gapus	—	—	—				
Sandejas A	+	+	+	+	+	+	±
Sandejas B	+	+	+	+	+	+	±
Carolina	—	—	—				
Bilibid	—	—	—				
King A	—	—	—				
King B	—	—	—				
B. Robles	—	—	—				
869	—	—	—				
568	—	—	—				
371	—	—	—				
75	—	—	—				
48	+	+	+	+	+	+	±
21	—	—	—				

TABLE II.—*Agglutination tests*—Continued.

Culture.	Serum Orani.							
	1-10.	1-20.	1-100.	1-500.	1-1,000.	1-2,000.	1-4,000.	1-8,000.
Abalogan	—	—	------	------	------	------	------	------
Berezosa	—	—	------	------	------	------	------	------
Leon	—	—	------	------	------	------	------	------
Solitana	—	—	------	------	------	------	------	------
Ramon	—	—	------	------	------	------	------	------
Lucero	—	—	------	------	------	------	------	------
C. Robles	—	—	------	------	------	------	------	------
Dizon	—	—	------	------	------	------	------	------
Anicete	—	—	------	------	------	------	------	------
Maquio	—	—	------	------	------	------	------	------
Sucgana	—	—	------	------	------	------	------	------
Calderon	—	—	------	------	------	------	------	------
135	—	—	------	------	------	------	------	------
Iris	—	—	------	------	------	------	------	------
Notbil	—	—	------	------	------	------	------	------
Sta. Monica	—	—	------	------	------	------	------	------
Sande	—	—	------	------	------	------	------	------
Malabon	+	—	------	------	------	------	------	------
Hagonoy	—	—	------	------	------	------	------	------
Orani	+	+	+	+	+	+	+	+
Navotas A	—	—	------	------	------	------	------	------
Navotas B	—	—	------	------	------	------	------	------
Sandejas A	—	—	------	------	------	------	------	------
Sandejas B	—	—	------	------	------	------	------	------
Bilibid	—	—	------	------	------	------	------	------
Gapus	—	—	------	------	------	------	------	------
B. Robles	—	—	------	------	------	------	------	------
King A	—	—	------	------	------	------	------	------
King B	—	—	------	------	------	------	------	------
869	—	—	------	------	------	------	------	------
568	—	—	------	------	------	------	------	------
371	—	—	------	------	------	------	------	------
75	—	—	------	------	------	------	------	------
48	—	—	------	------	------	------	------	------
21	—	—	------	------	------	------	------	------

TABLE II.—*Agglutination tests*—Continued.

Culture.	Serum Notbil.					
	1-20.	1-50.	1-100.	1-200.	1-500.	1-1,000.
Abalogan	—	—				
Berzosa	—	—				
Leon	—	—				
Solitana	—	—				
Ramon	—	—				
Lucero	—	—				
C. Robles	—	—				
Dizon	—	—				
Anicete	—	—				
Maquio	—	—				
Sucgana	—	—				
Calderon	—	—				
135	+	—				
Iris	+	—	—			
Notbil	+	+	+	+	+	±
Sta. Monica	+	+	+	+	—	—
Sande	+	+	+	+	+	±
Malabon	+	+	—			
Hagonoy	±	—	—			
Orani	—	—				
Navotas A	—	—				
Navotas B	—	—				
Sandejas A	—	—				
Sandejas B	—	—				
Gapus	—	—				
Bilibid	—	—	—			
B. Robles	+	—	—			
King A	—	—	—			
King B						
869	—	—				
568	—	—				
371	—	—				
75	+	+	+	—		
48	—	—				
21	—	—				

TABLE II.—*Agglutination tests*—Continued.

Culture.	Normal serum, 1-10.	Serum Santa Monica.							
		1-20.	1-50.	1-100.	1-200.	1-300.	1-400.	1-500.	1-1,000.
Abalogan	—			—	—	—	—	—	
Berezosa	—					—	—	—	
Leon	—					—	—	—	
Soletana	—				—	—	—	—	
Ramon	—					—	—	—	
Sucero	—					—	—	—	
G. Robles	—					—	—	—	
Dizon	—					—	—	—	
Anicete	—						—	—	
Ma[illegible]uio	—						—	—	
Sucgang	—						—	—	
Calderon	—						—	—	
135	—			—			—	—	
Iris	—	—	—	—	—		—	—	—
Notbil	±	+	+	+	+	±	±	—	—
Sande	—	+	+	+	+		+	+	+
Sta. Monica	—	+	+	+	+	+	+	+	+
Malabon	+	+	+	+					
Hagonoy	—	±	—	—					
Orani	—	—		—					
Navotas A	—	—		—					
Navotas B									
136 B	—	±		—					
136 A	—	±		—					
King A	—						—	—	
Gapus	—	—		—					
B. Robles	—			—					
Carolina	—	—	—	—	—			—	—
Bilibid	—	—	—	—	—		—	—	—
869	—	—	—	—					
568	—	—	—	—					
371	—	—	—	—					
75	—	+	+	+	±	—		—	—
48	—	±	—	—					
21	—	—		—					

Agglutination.—Various observers have noted a delayed or slow agglutination and spontaneous agglutination of certain strains. The results of agglutination usually were noted by us after the tubes had been placed for one to two hours in the thermostat at 37°, and for three hours at room temperature. One cholera strain reached the limit of agglutination only after twenty-four hours; two others only after twelve hours; the rest were positive within three hours. With all fresh cholera strains the results could be noted within three hours. One noncholera and one cholera strain were discarded because of their tendency to spontaneous agglutination. These organisms had been kept upon laboratory media for many months.

We found no instance of spontaneous agglutination, delayed agglutination, or diminished agglutination when working with fresh cholera strains, but in every instance they agglutinated promptly to the limit of the specific serum and showed no tendency to spontaneous agglutination in salt solution or serum other than specific cholera serum.

Marked differences in the agglutinability of various cholera strains of similar virulence usually does not exist. However, the four strains, Abalogan, Berezosa, León and Solitana, required for agglutination much stronger concentrations of cholera sera than the other cholera strains.

These were supposed to be strains of true cholera. They had been isolated from typical cholera cases and agglutinated in the routine manner by cholera serum in a dilution of 1–200. They were kept in ordinary agar medium and transplanted about once each month during July, August, September, and October. In November, cholera serum Regala II agglutinated all of the other cholera strains in a dilution of 1–2,000 + and did not agglutinate the four above mentioned in any dilution weaker than 1–200.

These cultures were carefully plated and the serum test repeated, with the same result. Each of the four produces in a rabbit a serum which agglutinates the homologous vibrio; the other three strangely acting vibrios, and all the cholera strains, in dilutions of from 1–1,000 to 1–2,000.

Four new cholera sera were prepared from the freshly isolated cholera strains, numbered 2, 4, 5 and 6, and the results may be seen in Table II. With these fresh sera (numbered 2, 4, 5, and 6) it will be noted that the strains Abalogan, León, and Solitana were not affected in the same manner as other cholera strains, although the differences were not so great as that shown by serum Regala II.

The lowered agglutinability of these four strains was not in evidence with all cholera sera. With the four homologous sera, and with one of the *El Tor* sera (King B), these strains were agglutinated to the limit.

It can not be said that the agglutinability always bears a fixed relation to the virulence of an organism. Old, avirulent laboratory cultures, Pfeiffer, Hankin, etc., are particularly susceptible to cholera sera; agglutinating in weaker dilutions than recently isolated strains.

HAEMOLYTIC PROPERTIES.

The hæmolysing quality of certain vibrios has been the cause of much discussion.

Ruffer (10) upon this group considers the *El Tor* vibrio to be distinct from cholera, as none of his cholera strains possessed hæmolysing properties. Kolle and

Meinicke(5), Muhlens and Von Raven(7), Schumacker(11), Neufeld and Hændel(8), demonstrated that certain cholera strains possessed hæmolysing properties. These workers used cultures which had been kept for a considerable time upon laboratory media. Kraus(6), working with fresh cholera cultures, was unable to find a strain with hæmolysing properties.

The hæmolytic action of our vibrios was tested by the simple method employed by Ruffer and also by the method of Kraus. One loop of an eighteen-hour culture was suspended in 5 cubic centimeters of normal salt solution. To 0.5 cubic centimeter of this suspension, 0.5 cubic centimeter of a 5 per cent suspension of well-washed blood corpuscles was added. The mixture was placed in the thermostat at 37° and results noted after two hours, four hours, and twenty-four hours. This method was also used by Neufeld and Hændel. By this means Ruffer found no strain of cholera with hæmolytic properties, while Neufeld and Hædel found that several cholera strains were capable of producing hæmolysis. However, none of these were freshly isolated.

Our cholera strains, both fresh and old, uniformly failed to produce hæmolysis with these methods. Both *El Tor* strains examined were hæmolytic, as well as 18 of the 22 noncholera vibrios. The results are shown by Table III.

TABLE III.—*Hæmolytic tests.*

NONCHOLERA VIBRIOS.

Name of culture.	Ruffer's method, suspension of live vibrios.			Kraus's method, 0. 1 cc. 3-day bouillon, killed to 1 cc. 5 per cent suspension red cells.		
	2 hours.	4 hours.	24 hours.	2 hours.	4 hours.	24 hours.
Iris	+	+ +	+ + +	----------	+	+ +
Notbil	+	+ +	+ + +	----------	+	+ +
Sande	----------	+	+ + +	----------	+ +	+ + +
Malabon	+	+ + +	----------	----------	+	+ +
Sta. Monica	+	+ +	+ + +	----------	+ +	+ + +
Hagonoy	+	+ +	+ + +	----------	+ +	+ + +
Orani	—	—	—	----------	—	—
Carolina	—	—	—	----------	—	—
135	—	—	—	----------	—	—
Navotas A	+	+ +	+ + +	----------	tr.	+
Navotas B	+	+ +	+ + +	----------	tr.	+
Sandejas A	+	+ +	+ + +	----------	tr.	+
Sandejas B	+	+ +	+ + +	----------	tr.	+
Gapus	+ +	+ + +	----------	tr.	+ +	+ + +
Bilibid	—	+	+ +	—	tr.	+
869	----------	+	+ + +	----------	+	+ +
846	+	+ +	+ + +	----------	+	+ +
568	----------	+	+ + +	----------	+	+ +
371	—	—	—	—	—	—
75	+	+ +	+ + +	----------	+	+ +
48	+	+ +	+ + +	----------	+	+ +
21	----------	+	+ + +	----------	—	+

TABLE III.—*Hæmolytic tests*—Continued.

CHOLERA VIBRIOS.

Name of culture.	Ruffer's method, suspension of live vibrios.			Kraus's method, 0.1 cc. 3-day bouillon, killed to 1 cc. 5 per cent suspension red cells.		
	12 hours.	24 hours.	48 hours.	12 hours.	24 hours.	48 hours.
King A (El Tor)	+ +	+ + +				
King B (El Tor)	+ +	+ + +				
Abalogan	−	−	−			
Berezosa	−	−	−			
Leon	−	−	−			
Solitana	−	−	−			
1131	−	−	−			
1108	−	−	−			
1104	−	−	−			
1101	−	−	−			
1051	−	−	−			
1038	−	−	−			
1029	−	−	−			
955	−	−	−			
954	−	−	−			
953	−	−	−			
952	−	−	−			
1021	−	−	−			
758	−	−	−			
664	−	−	−			
622	−	−	−			
545	−	−	−			
492	−	−	−			
Cavite I	−	−	−			
Cavite II	−	−	−			
Lorenzo C.	−	−	−			
Santiago	−	−	−			
No. 4 Taytay	−	−	−			
Miraflores	−	−	−			
Bautista	−	−	−			
B. Robles	−	−	−			
Suing	−	−	−			
No. 30	−	−	−			
Salas	−	−	−			
Regala I	−	−	−			
Regala II	−	−	−			
David	−	−	−			
Nicolas	−	−	−			
Camay	−	−	−			
Ramon	−	−	−			
Sucero	−	−	−			
C. Robles	−	−	−			
Sucgang	−	−	−			
Dizon	−	−	−			
Aniceto	−	−	−			
Maquio	−	−	−			
Calderon	−	−	−			
No. 2	−	−	−			

TABLE III.—*Hæmolytic tests*—Continued.

Name of culture.	Ruffer's method, suspension of live vibrios.			Kraus's method 0.1 cc. 3-day bouillon, killed to 1 cc. 5 per cent suspension red cells.		
	12 hours.	24 hours.	48 hours.	12 hours.	24 hours.	48 hours.
No. 3	—	—	—			
No. 4	—	—	—			
No. 5	—	—	—			
No. 6	—	—	—			
902	—	—	—			
Betonio	—	—	—			
Caballeros	—	—	—			
Mendoza	—	—	—			
046	—	—	—			
074	—	—	—			
099	—	—	—			
125	—	—	—			
Zacarias	—	—	—			
Salvador	—	—	—			
Tarlac	—	—	—			
Lloret	—	—	—			

DOES THE HOG ACT AS A "CHOLERA CARRIER" IN THE PHILIPPINES?

Because of the extent to which the hog acts as a scavenger in this Archipelago, it seemed advisable to determine whether or not that animal could act as a cholera carrier under natural conditions. Accordingly, two partly grown pigs were selected for feeding, while a third was chosen as a control.

After carefully ascertaining that there were no cholera-like vibrios in the stools of any of the animals, two were fed three twenty-four hour agar slants of a recently isolated cholera vibrio, mixed with fæces from a normal man and made faintly alkaline with sodium carbonate. The stools of these two pigs were examined daily for a week, but we were never able to isolate a vibrio from them. The experiment was repeated on the same animals with the same result. Finally, each one of the pigs was fed a litre of fresh rice water stool from cases of cholera in San Lazaro Hospital. Neither showed any bad effects from the feeding and again we were unable to isolate a vibrio from the fæces from either pig in an examination made each day for ten days. As we were endeavoring to simulate natural conditions, we did not try the effect of neutralizing the contents of the pigs' stomachs, nor similar procedures.

SUMMARY.

We have not been able to add anything to what is already known to questions numbered (1) and (2). Every vibrio in our list which agglutinates in a 1 to 200 dilution of specific anticholera serum is a cholera vibrio, while none of the noncholera vibrios agglutinated in a weaker dilution than 1 to 10. On the other hand, four of our cholera vibrios did not agglutinate equally with all of our cholera sera; with some they did not agglutinate in a weaker dilution than 1 to 200. It is noted that three of these vibrios had been in mixed cultures on agar for about seven days, in transit from the provinces, but whether this had anything to do with their lowered agglutinability we are not prepared to state.

None of our agglutinating strains were hæmolytic, so that we have not found any vibrios of the *El Tor* type in these Islands.

We have not been able to make "cholera-like" vibrios acquire agglutinability with cholera sera.

Dieudonné's medium is satisfactory for the isolation of cholera vibrios from the stools, but it does not assist in separating cholera vibrios from "cholera-like" vibrios.

We have not been able to show that the hog acts as a "cholera carrier" under as nearly natural conditions as possible.

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THE SPECIFIC CURE OF YAWS WITH DIOXY-DIAMIDO-ARSENOBENZOL.[1]

By RICHARD P. STRONG.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

In certain portions of the Philippine Islands yaws, or frambœsia,[2] is a very common disease. In some of the smaller towns lying near Manila, for example Parañaque, Las Piñas and Bacoor, it occurs much more frequently in children than in adults, a considerable percentage of the former being infected. In the course of a search of an hour or two I was able to find in the neighborhood of a dozen or more cases of this disease in each of these villages.

The disease is not only highly disfiguring, but it is very contagious and usually runs a chronic course, frequently preventing the patient from working and sometimes eventually disabling him. The treatment hitherto has been most unsatisfactory and usually must be very prolonged before success is obtained. While cures after long periods have frequently resulted among the better classes affected, as a rule the disease is one of very long duration and yields but slowly to medication. Some of the cases reported in this paper demonstrate these points. Even the patients who can be seen in the dispensary and hospital as a rule become discouraged with the treatment long before a cure results, and usually abandon it. The successful treatment of this disease in the cases among the lower classes frequently encountered in the smaller towns hitherto has been entirely impracticable, for the reason that it usually has been impossible to persuade and also to cause individuals to take a prolonged course of medication, which, to be successful ultimately, frequently must be pursued for many months.

Manson states that yaws runs a chronic course and lasts for weeks, months, and years. The duration depends on the general health and idiosyncrasies of the patient as well as on his hygienic conditions and the treatment employed.

According to Daniels the usual duration of the disease is two or three years, but on the parts of the body where the epidermis is thick, such as the soles of the feet, it may persist for much longer periods.

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[1] Preliminary remarks on this subject were made before the Manila Medical Society on September 5, 1910, where photographs and one of the cured patients were presented.

[2] Commonly known among the natives as *bubas*.

Scheube believes that the duration of yaws varies between a few weeks and several years, and that the treatment, food and hygienic condition of the patient influences the time.

According to Castellani, unless the disease becomes extinct after the secondary stage, it may extend to many years. Jeanselme states that framboesia runs a chronic course varying from several weeks or months to a number of years. Firth describes yaws as a chronic disease, the secondary eruption lasting from a few months to two years.

THE SPECIFIC CHARACTER OF YAWS.

It is not my intention here to enter into a prolonged discussion of the question of the specificity of yaws as a disease. Almost all observers agree that it is not identical with syphilis. Sheube and Firth are inclined to support the original idea of Hutchinson that yaws was the original disease from which European syphilis has been evolved or that the two diseases developed from a parent form, each having been modified by being propagated by different races in different climates. Manson, Castellani, Jeanselme and Plehn regard them as specifically distinct.

I have had abundant opportunity for the observation of all forms of yaws in several tropical countries for a number of years and my own opinion, based largely upon clinical material, histologic examinations, experiments in inoculation and serum reactions carried on in this laboratory, as well as upon the experimental work of others, is strongly in favor of the view that yaws and syphilis are distinct.

I believe that while the two diseases are certainly closely related from an etiologic standpoint, yet they are different affections. Since the discovery of the specific organism of yaws, *Treponema pertenuis*, by Castellani in 1905, a number of observers have carried on comparative morphologic studies between this organism and *Treponema pallidum*.

Prowazek, Blanchard, Martin and Levaditi have discussed the slight morphologic differences between these organisms; these however are not sufficiently constant or definite to serve as a means of differentiation. On the other hand, inoculation experiments, both in man and animals, appear to have resulted in a more definite distinction. Charlouis in 1881 inoculated a native suffering from typical yaws, with syphilis. A primary indurated syphilitic chancre developed, and a typical secondary syphilitic eruption followed. This experiment apparently has not been repeated in man, although a number of observers, Bestion, Powell, A. Nicholls and others, have reported cases of yaws which subsequently have contracted syphilis.

Neisser, Baermann, Halberstädter, and Castellani have shown that monkeys successfully inoculated with framboesia do not thereby become immune to syphilis, and subsequently may be infected with the latter disease and vice versa, apes successfully inoculated with syphilis remain susceptible to framboesia. Halberstädter also believes the appearances of the primary inoculative lesion in lues and framboesia to be different. All of these authors conclude from their experiments that the two diseases are etiologically distinct.

Levaditi states that monkeys immunized against yaws do not acquire any immunity for syphilis, but monkeys immunized against syphilis acquire partial immunization for frambœsia. Ashburn and Craig found that monkeys of the species *Cynomolgus philippinensis* Geoff. are susceptible to yaws, but not to syphilis.

Castellani applied the Bordet-Gengou complement fixation reaction to yaws and concluded from his experiments that it was possible to demonstrate the existence of specific yaws antibodies and antigen. The technique he employed was similar to the usual one recommended by Wassermann, Neisser and Bruck. Goat's corpuscles and rabbit's hæmolytic serum were used. When extracts of yaws papules were added to serum from monkeys which had been inoculated successfully with yaws, the reaction was positive. When the reaction was performed with extract of syphilitic condylomata, or extract of a primary syphilitic sore (in place of an extract of yaws papules) and with yaws serum, the reaction was negative; also, when performed with extract of yaws papules and with serum from a monkey immunized for syphilis, the reaction was negative. From these and other experiments, Castellani concluded that it is possible to detect specific antigen in the yaws papules and in the spleens of cases of yaws; and specific yaws antibodies in the blood of monkeys treated by inoculation with yaws material; also that yaws antibodies and antigen are different from syphilitic antibodies and antigen, and therefore syphilis and yaws differ specifically.

Bowman, in this laboratory, also performed a few experiments with the complement binding reaction in cases of ayaws and syphilis. He found in the usual way as suggested by Landsteiner, Neisser and Poetzl, that when an extract of guinea pig's heart was added to the serum from a case of syphilis, the reaction was positive. Red blood cells of the ox and immune hæmolytic rabbit serum were employed. On the contrary, when the extract of the guinea pig's heart was added to a serum from a human case of yaws, the reaction was negative. When extract of yaws papules was added to serum from yaws patients, the reaction was positive. Bowman concludes that the serum from cases of yaws does not bind complement when the extract from a guinea pig's heart is used, and that his experiments furnish additional evidence of the nonidentity of syphilis and yaws.

Hoffman, on the other hand, reported a case of yaws in which Blumenthal found the Wassermann reaction positive. Ziemann did not think the diagnosis of this case definite.

There seems little doubt but that cases of syphilis have sometimes been diagnosed as those of yaws, and in some of the recent literature pictures are found of cases diagnosed as yaws in which the lesions appear to resemble rather those of syphilis and in which the diagnosis of yaws from the pictures would seem hardly justified.

While this article was in the course of preparation, H. Nichols' articles in the "Journal of Experimental Medicine" and "Journal of the American Medical Association" were received. Nichols reports that rabbits can be infected in the testicle with the spirochætæ of yaws, and that the complement fixation reaction has been tried on rabbits so infected and has been positive in several cases.[3] In the experiment he employed acetone insoluble liver extract as antigen, and the human corpuscle and rabbit hæmolytic system. On the other hand, the reaction failed in his hands in the case of a negro suffering from yaws and in two monkeys infected with the same disease.

Bruck reported a positive Wassermann reaction in a patient who gave a history of having had yaws five years before. However, it appears that the observer would hardly be justified in drawing definite conclusions in regard to the diagnosis of this case since the lesions might have been those of syphilis.

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[3] He also reports the favorable influence of dioxy-diamido-arsenobenzol on the experimental lesions produced in the testicles of four of these rabbits.

Until we have more information on the question of the complement binding reaction, it would be unwise to draw any absolute conclusion from the result of the experiments with it in relation to yaws and syphilis.

However, from the other data submitted it is believed that the specificity of yaws as a disease has been shown and it is not deemed necessary here to present further the evidence based upon clinical and pathologic observation.

TREATMENT FORMERLY RECOMMENDED.

The consensus of opinion of those who have had a wide personal experience with yaws is that the treatment of the disease is usually unsatisfactory.

Manson writes:

> All are agreed as to the propriety of endeavoring by good food, tonics and occasional aperients to improve the general health. Most are agreed as to the propriety of endeavoring to procure a copious eruption by stimulating the functions of the skin by warm demulcent drinks; by a daily warm bath with plenty of soap; and, during the outcoming of the eruption, by such diaphoretics as liquor ammoniæ acetatis, guaiacum, etc. Confection of sulphur is also recommended as a suitable aperient; it may be taken frequently in the early stages of the disease. All are agreed as to the propriety of avoiding everything—such as chill—tending to repress the eruption; warm clothing is therefore indicated. Many use mercury, or potassium iodide, or both, after the eruption is fully developed. These drugs have undoubtedly the power of causing the eruption in yaws to resolve. Some practitioners rarely use them, or, if they do so, only at the latest stages of the disease considering that relapses are more prone to occur after their too early employment. Mercury, owing to its proneness to cause anæmia, is less frequently employed than potassium iodide. Where the eruption is persistently squamous, or papular, arsenic is frequently prescribed. Some touch the yaws with sulphate of copper; some apply nitrate of mercury ointment; others iodoform ointment; others leave them alone, confining their local measures to the enforcement of cleanliness. When the soles of the feet are attacked, the feet ought to be soaked in warm water to soften the epidermis, which should then be cut away sufficiently to liberate the subjacent yaw. Ulceration must be treated on ordinary principles. During convalescence, iron, arsenic and quinine are indicated.

Scheube favors internal treatment with mercury and iodide, and states that Schuffner has communicated to him that the small number of cases which do not yield to such treatment are usually very favorably influenced by Zittmann's decoction. After antisyphilitic treatment, arsenic is recommended, particularly in weak and anæmic patients. Local solutions of sublimate, and touching with carbolic acid, nitric acid, mercuric nitrate, copper sulphate, silver nitrate, applications of tincture of iodine, iodoform ointment or oil, and mercuric salve are recommended. In cases with excrescences of long duration, curetting with a sharp spoon, or removal with the scissors, is also advised. Scheube mentions that Mense found a watery paste of bismuth subnitrate most successful for local application, while Hirsch recommends one part of lactic acid and eight parts of nitrate of mercury ointment for this purpose.

Plehn states that mercury and iodide should in all cases be tried. Cauterization of the lesions with a hot iron or sharp curetting of them is not recommended. Bismuth paste is preferred for local treatment. In native children calomel powder is advised for internal administration several times daily in doses of 0.002 to 0.01 gram, according to the age. In case the eruption is not too extensive, it is recommended to cover the lesions with calomel powder or grey salve. Painting with a thin paste of calomel and salt water is also advised. For ulcerating granulomata about the lips or corners of the mouth an alcoholic sublimate solution 1 to 100 or 20 to 30 per cent chromic acid solution is recommended. A continuation of the treatment after disappearance of the lesions, in order to prevent their return is not thought to be necessary.

Castellani states, the long duration of frambœsia and its great contagiousness render it a serious malady. Patients suffering from it are unable to attend to their work. In Ceylon the majority of European practitioners use mercury and potassium iodide. Others affirm these drugs to be quite useless, and believe that cleanliness and good and abundant food are quite sufficient to bring about a cure. In Castellani's clinic the conclusion arrived at was that potassium iodide was the most effective means of treatment. He states that some cases may recover spontaneously, but this is certainly the exception, not the rule. The potassium iodide should be given in large doses; in adults, 15 grains (1 gram) and in children 5 grains (0.33 gram), three times daily. Occasional cases are met with refractory to treatment, and tertiary lesions are often intractable. Mercury is of very little use as a rule. In some very stubborn cases a course of potassium iodide, followed by one of atoxyl injections is recommended. Castellani further states:—'An important point often overlooked by the practitioner is that the treatment should be prolonged for a considerable time after the complete disappearance of the eruption, inasmuch as clinical experience, as well as experiments on inoculated monkeys, prove that the specific treponemata may, and do persist in the lymphatic glands and internal organs long after the cutaneous manifestations have disappeared. Local treatment consists chiefly in keeping the skin scrupulously clean, washing the eruption twice daily with a perchloride of mercury solution (1 to 1,000) which greatly allays the itching. The ulcerated lesions may be dusted with iodoform, europhen, or boracic acid. Mercury ointments may be beneficial, but in our experience are not sufficient to hinder secondary pyogenic infections. Caustics are not called for unless the ulcers become phagedenic. In such cases pure carbolic acid is best. Though the external treatment may be useful, one must bear in mind that it is not, as a rule, sufficient alone to cure the disease.'

Jeanselme believes that mercurial treatment has a certain influence upon yaws, but it does not prevent relapses. The author treated sixteen children from 3 to 12 years of age with mercury. They took regularly during fifteen days from two to four teaspoonfuls of "liqueur de Van-Swieten," according to the age of the child. The lesions dried up rapidly, and became covered with thin, sulphur-yellow crusts. When the author was obliged to terminate the experiment, five of the patients had a clear skin; the lesions in nine patients were visibly ameliorated; only two of the children did not receive any benefit from the treatment. Dressings and lotions of sublimate are said to influence very favorably the eruption. Jeanselme states that potassium iodide employed in the same doses as in syphilis has an unquestionable action upon yaws. It causes the eruption rapidly to recede. In obstinate cases cauterization of the vegetative ulcerations with sulphate of copper, with acid nitrate of mercury, and scraping with a curette, following with igneous cauterization, gives good results.

Firth states the first essential in the actual treatment of the attack to be the cleansing of the patient by means of warm baths and soap. Special care must be taken to avoid chills, as exposure to cold often causes a disappearance of the eruption, accompanied by much constitutional disturbance. The food must be nourishing, consisting of fresh meat, fish, rice, yams, and diluent drinks, combined with medicinal tonics. Locally, disinfectant lotions of boric or carbolic acids, or of corrosive sublimate, are of the first importance. The acid reaction of the secretion from yaws tubercles has suggested the use of alkali as a local dressing. Both Modder and Rat state that excellent results follow the use of lotions containing either bicarbonate of soda or carbonate of ammonia of the strength of ten grains to the ounce. Sulphate of copper is efficacious as a topical application; so likewise are iodoform and weak nitrate of mercury ointment. The use of mercury in this disease needs the utmost care and supervision, as its abuse has been largely responsible in the past for the severity and fatality of many cases; *it can not be regarded as a specific remedy for the disease, as it is for syphilis*, but, given in minute doses for a short time, mercury seems to act as a beneficial alterative. Of other internal remedies, iodide of potassium with arsenic is very valuable, while in some cases iron and sulphocarbolate of calcium are of the greatest benefit. Arsenic is very successful in the cases in which the eruption is badly developed or scaly, as in the *pian darte* variety. When the feet and hands are affected, prolonged soaking in hot water is often required in order to soften and remove the thick epidermis; the exposed yaws growth can then successfully be treated on the lines indicated above. During convalescence iron and arsenic should both be administered over long periods; while in all stages of the affection perfect cleanliness and the best hygienic conditions are needed, both for the sake of the sick and of those brought into contact with them.

Woolley recommends potassium iodide internally and local applications of bichloride of mercury followed by iodoform.

Daniels states that probably no drug influences the duration of the disease. Mercury and arsenic certainly do not. Potassium iodide is uncertain in its action. The eruption will sometimes disappear rapidly when iodides are given, but even in such cases when the use of the drug is continued, fresh eruptions appear. The use of iodide is therefore limited. Local applications that merely serve to keep the granuloma clean are valuable, but escharotics and irritants, although they may destroy the yaws, are likely to cause the formation of scars. The painful granulomata on the feet are best removed by the action of nitric acid, acid nitrate of mercury, or silver nitrate.

From this summary of the literature of the treatment of the disease, it appears that a number of eminent authors regard its local treatment as very important, and that even the most successful drug (potassium iodide) frequently fails to produce a cure, and that in many cases the treatment of yaws, to be successful, must be a very prolonged one.

SPECIFIC TREATMENT OF YAWS.

A few months ago, through the kindness of Professor Ehrlich, I received a shipment of dioxy-diamido-arsenobenzol[4] for use for experimental purposes in syphilis. I take great pleasure in publicly acknowl-

[4] $(NH_2 . OH . C_6H_3 . As : As . C_6H_3 . OH . NH_2)$.

edging my thanks to him for the opportunity to try the effect of this very valuable preparation. Because of the favorable results which were being obtained with it in the treatment of syphilis, the idea naturally suggested itself to try the remedy in yaws on account of the morphological and biological relationship which exists between the spirochætæ giving rise to these two diseases. Twenty-five cases in all have been studied and treated. A report of the cure of three of the most striking of these was made before the Manila Medical Society on September 5, where photographs and one of the patients were exhibited. The discussion of all of the work has been withheld until the present time, in order to ascertain if relapses would occur. So far there has been no evidence of a relapse, and the cases have all remained cured, although the great majority of them were treated over four months ago.

The preparation was received in hermetically sealed capsules. These were opened, and the solution always prepared immediately before being inoculated. Dioxy-diamido-arsenobenzol, as Ehrlich has stated, is not readily soluble, and to obtain a satisfactory solution for inoculation, his suggestion as to the most satisfactory means for the solution of the monochlorhydrate was followed. From 0.3 to 0.4 gram of the preparation was placed in a glass vessel, moistened with a few drops of methyl alcohol, and thoroughly rubbed up with a glass rod. From 20 to 30 cubic centimeters of distilled water were then added, the stirring with the glass rod being continued. When the solution was apparently complete, 5.5 cubic centimeters (for 0.3 gram of the preparation) of an $\frac{N}{10}$ sodium hydroxide solution were slowly added, stirring with the glass rod being continued. The precipitate, which forms on this addition, was then slowly redissolved.

The injections were given deep into the gluteal muscles, from 15 to 20 cubic centimeters of fluid usually being injected in one place. On the following day and the day after there was usually some reddening, swelling and induration of the skin and underlying tissues in the vicinity of the point of the inoculation. In no instance did suppuration result, nor any unfavorable symptoms develop. Occasionally a transitory rise of temperature was noted a few days after the injection. In some of the cases, pain was complained of after the injection, sometimes lasting for from 10 to 24 hours, or sometimes even longer, but as a rule no great complaint was made. A number of the inoculated cases have been among young children who did not cry, either during the inoculation or after it; usually they did not care to play about for the first 24 hours following the injection. One European suffering with syphilis who was given a large injection into the buttock, suffered severe pain, lasting for nearly 24 hours. This case was given a second injection intravenously twenty days later. No pain whatever followed.

It was found that in every instance for the cases of yaws treated a single injection of the drug was sufficient to produce a cure, even though a number of them showed tertiary lesions with ulcerations. No local treatment was used with any of the patients, nor was any other treatment internal or otherwise administered after the injection. A few cases had previously been treated with iodides; these were discontinued a few days before the injection of dioxy-diamido-arsenobenzol was given.

NOTES OF THE CASES TREATED.

The notes of the cases treated are as follows. Photographs before and after treatment frequently were secured where opportunity was favorable.

Case I.—(Plates I and II.) Felixberto; male, age 11 years. Diagnosis, yaws secondary stage; duration of the disease, about one year.

The lesions are situated anteriorly over the forehead, nose, cheeks, upper lip, chin, chest, upper arms and forearms, thighs and legs. These consist of raised, mushroom-like, sharply circumscribed granulomata measuring from 1 to 5 centimeters in diameter and about 1 to 1.5 centimeters in thickness. They are in general circular in outline. Frequently the lesions have coalesced. On the right ankle is an excoriated lesion apparently the result of traumatism, and on the right forearm just above the wrist is an ulcerated granuloma. The patient has been under treatment at the St. Luke's dispensary for the past two months. For about seven weeks he has taken five grains of potassium iodide three times daily. Before this he took syrup of iodide of iron. Locally, he was treated with bichloride and salicylic acid dressings, these being applied every few days. The treatment has apparently had no effect whatever on the disease. A smear from one of the granuloma stained with Giemsa's solution showed a few spirochætæ. Plate I shows the patient as he appeared after two months of the treatment as described above. All of these measures were then discontinued and the patient given an injection of a solution of 0.28 gram of dioxy-diamido-arsenobenzol, half of the solution being injected into each buttock. On the fourth day after the injection it was reported that the lesions were disappearing. The patient was seen by the author one week after the injection. The granulomatous lesions had almost entirely disappeared. In twelve days the skin was perfectly smooth; the lesions had entirely disappeared, and only pigmentation of the skin remained where the granulomatous lesions formerly existed. Plate II represents a photograph taken at this time. The skin was everywhere perfectly smooth. Examination of the urine one week after the injection showed it to be normal. The case since has remained entirely well.[5]

Case II.—(Plates III and IV.) Gonzales; male, age 5 years; duration of the disease 8 months. The lesions are scattered over almost the entire face, neck, upper arms and forearms, hypogastric region, thighs, legs, ankles, and feet; posteriorly over the neck, shoulders, arms and forearms, back, buttocks, thighs, legs and ankles. The chest and abdomen are particularly clear. The lesions consist of granulomata measuring usually from about 0.3 to 1.5 centimeters in diameter, being slightly raised above the skin and being covered, particularly on the face by yellow crusts. On the arms, forearms and legs, the lesions are more distinctly papular in character. A smear from one of these papules shows spirochætæ. This child had been treated previously with native remedies but with no favorable results (see Plate III). He was given an injection of 0.25 gram dioxy-diamido-arsenobenzol dissolved in 20 cubic centimeters distilled water, one-half of the amount being injected deeply into each buttock. Nine days later the lesions had completely disappeared, as may be seen from Plate IV, which was taken at that time. The skin was then everywhere clean and smooth, and only pigmented patches, more marked on the legs and arms, remained as an evidence of the pre-existing lesions. There has been no relapse, and the patient since has remained entirely well.

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[5] I am indebted to Dr. Eleanor Pond of St. Luke's Dispensary for having notified me of this case.

Case III.—(Plates V and VI.) Fausto; male, age 9 years; states duration of the disease about two months. The lesions are situated on the forehead, neck, shoulders, left arm, at the bend of each elbow, forearms, thighs and legs, and posteriorly over the back, buttocks, thighs, popliteal spaces, legs and ankles. They consist of granulomatous tumors and papules sharply circumscribed, measuring from about 4 or 5 millimeters to about 4 centimeters in diameter. On the forehead and neck the lesions measure about 4 centimeters in diameter, and are distinctly granulomatous and raised for a distance of about 0.5 centimeter above the surrounding skin. The same character of lesion, although smaller in diameter, occurs at the bend of the elbows and over the region of the left popliteal spaces; elsewhere the lesions are more distinctly papular in character. On the left heel is an ulcerating granulomatous lesion (see Plate V). A smear from one of the papules shows spirochætæ. There are two other members of this boy's family afflicted with yaws, the father and brother. The brother's condition is reported as Case No. IV. The present patient was injected with 0.3 gram of dioxy-diamido-arsenobenzol in 20 cubic centimeters distilled water, the injuction being given into the buttocks in the usual manner. Nine days later the lesions had practically disappeared. Dry, scaly patches remained in the left popliteal space, and anteriorly at the bend of the elbows and over one spot on the neck. The lesion on the left foot was covered by a clean scab. These scaly patches had disappeared, and the ulcer on the heel entirely healed, five days later. (See Plate VI.) The case since has remained entirely well.

Case IV.—(Plates VII and VIII.) Enrique; age 4 years; brother of Case III; duration of disease 2 years. The lesions are situated particularly about the lower lip and chin, the right axilla, bends of the elbows, forearms and thighs, and posteriorly in the right axillary fold, at the bends of the elbows, the gluteal fold, buttocks, popliteal spaces and legs. They consist of ulcerating granulomatous masses measuring 5 or 6 centimeters in diameter, raised in some instances a centimeter and a half above the surrounding skin, and partially covered by yellow crusts. There are large scars over the back of the legs, right thigh, ankle, and numerous small pigmented patches on the legs, arms and a few on the chest, the results of healed lesions (see Plate VII). Smears from the ulcerating lesions reveal several forms of bacteria and spirochætæ. The patient was given an injection of 0.28 gram of dioxy-diamido-arsenobenzol. Nine days later a very remarkable change had taken place in the lesions. These on the arms and legs were very greatly reduced in size, but had not entirely disappeared. However, the appearance of the remaining lesions was entirely unlike that of granulomata, they being composed mostly of contracted scar tissue. The lesions about the mouth had almost disappeared, a thin scab being visible on the chin. Some of these changes may be noted in the photograph, Plate VIII, fig. 1. Unfortunately, the photographer had not another plate with him so that no posterior view of the patient could be taken at this time. The patient was seen twelve days later and again examined and photographed (see Plate VIII, figs. 2 and 3). The lesions were then almost healed with the exception of a small scab at the bend of the left elbow anteriorly and another posteriorly, and a scab over the right popliteal space. The skin since has become entirely clean and the patient has remained well. The lesions in this case were of a most severe character.

Case V.—Apolonia; female, age 9 years; mother also infected (see Case IX); duration of the disease 4 years. The lesions consist of an ulcerated granuloma over the left ankle, apparently a tertiary lesion. Over the right internal malleolus there is a large fungating mass with much scar tissue about it; there are also granulomata about the toes and many scars and pigmented patches on the right leg. Above the knee on the left thigh there is a large scar measuring about 10 centimeters in diameter. There is also a large scar on the outside of the knee of the right leg. Over the chest, abdomen, and back there are numerous scars and patches of pigmented skin where previous lesions have apparently existed. Spirochætæ were present in a smear from one of the lesions. The patient was given 0.3 gram of dioxy-diamido-arsenobenzol, injected as usual into the buttocks. She could not be found nine days later, but was seen twenty days after the injection, when the granulomatous lesions had entirely healed, and she since has remained well.

Case VI.—Teodorica; female, age 6 years; duration of the disease 3 years. The lesions consist of an ulcerating granuloma on the left heel; pigmented patches over the buttocks, posterior surface of the left leg, and the abdomen. Over the sternum there is a scar measuring about 4 centimeters in diameter. There are also large scars over the right side of the neck, which are reddened and have evidently recently healed. There are two granulomata measuring about 3 and 4 centimeters in diameter on the right side of the neck and one of the left forearm measuring about 3 centimeters. A smear from one of these shows spirochætæ. The patient was given 0.28 gram of dioxy-diamido-arsenobenzol in the usual manner. Fifteen days later the granulomatous lesions had entirely disappeared. On the heel was a small clean scab. When seen one week later the heel also was perfectly clean. There has been no return of the eruption.

Case VII.—Ciriaco; male; age 16 years; duration of disease ten months. The lesions consist of an ulcerating granuloma situated above the right ankle, and measuring about 6 centimeters in diameter. Over the left external malleolus there is a small ulcerating patch measuring about 3 centimeters in diameter. There is also a small ulcerating granuloma over the left great toe. A smear from this shows spirochætæ and a few bacteria. There are pigmented patches scattered over the skin of the whole left leg and over the thigh. These patches are evidently the results of healed lesions. The chest and back are clear. The patient was given 0.3 gram of dioxy-diamido-arsenobenzol in the usual manner. He was seen nine days later, when the lesions had almost disappeared. Twenty days later they had entirely healed. He has since remained well.

Case VIII.—Buenaventura; age 10 years; duration of disease stated to be eight months. The lesions consist of a granulomatous ulcer situated above the left ankle, measuring about 5 centimeters in diameter. There are smaller ulcerated granulomata over the right ankle. There are pigmented patches over the knees and over the back of the thighs and legs. On the neck there are four papular tumors measuring about 1 centimeter in diameter. A smear from one of these shows spirochætæ. The patient was given 0.3 gram of the preparation in the usual manner, and when seen twenty days later the skin was smooth and the active lesions were entirely healed; there has been no return of them.

Case IX.—Maria; age 25 years; the mother of Case V; duration of disease (?). The lesions consist of four granulomata ranging from 2 to 4 centimeters in diameter, and situated on the buttocks and one within the gluteal fold. A smear from one of these revealed spirochætæ. The patient was injected with 0.4 gram of the preparation in the usual manner. Twenty days later the active lesions had entirely disappeared, leaving pigmented patches of smooth skin where they had formerly existed.

Case X.—Bernardo; male; age 22 years; duration of disease one and one-half years. There is an ulcer measuring 3 centimeters in diameter, evidently a tertiary lesion, situated on the left ankle and a small fungating mass on the left toe. There are numerous pigmented patches and scars over the posterior surface of the legs and back. Spirochætæ were found in a smear from the fungating mass. The patient was given 0.4 gram of the preparation by injection in the usual manner. Twenty days later the lesions had entirely healed. He since has remained well.

Case XI.—Tomas; age 11 years. The lesions consist of about thirty papillomata situated over the shoulders, arms, forearms and knees. They are sharply circumscribed, and measure from about 4 millimeters to 1 centimeter in diameter. A smear from one of these shows a few spirochætæ. Three-tenths of a gram of the preparation was injected into the buttocks in the usual manner. Ten days later the lesions had entirely disappeared, leaving only slightly pigmented areas where they had previously existed.

Case XII.—Castor; age 18 years; duration of disease about 1½ years. The lesions consist of granulomatous tumors measuring from 5 centimeters in diameter, situated anteriorly over the right ankle, over the right external malleolus, above the right knee, and posteriorly over the right ankle, over the left ankle, above the heel and above the left knee. They are usually covered by yellow crusts. Over the left elbow posteriorly and the right ankle there are old scars. A few spirochætæ were found in a smear from one of the granuloma. The patient was given 0.3 gram of the preparation in the usual manner. Fifteen days later the active lesions had entirely disappeared. I have not been able to see this patient since that date.

Case XIII.—(Plate IX.) Leon; age 12 years; duration of the disease a little over a year. No others in the family have yaws. The lesions are situated anteriorly over the forehead, neck, axillae, bends of the elbows, knees, legs, ankles, scrotum, penis and foreskin, posteriorly over the neck, shoulders, posterior surface of right arm and forearm, both elbows, back, left thigh, gluteal fold, posterior surface of legs and left heel. The lesions consist of granulomatous tumors varying in size from about 5 millimeters to 3 and 4 centimeters in diameter, usually covered by yellow crusts. On the lower legs a number of the granulomata are circular in outline, the skin in the center being depressed. Evidently ulcerations will occur in these central areas should the case remain untreated. There is an ulcer on the left heel measuring about 3 centimeters in diameter. On the scrotum, penis and foreskin there are 9 papillomata measuring about 4 to 5 millimeters in diameter. The granulomatous tumors are raised from 0.5 to 1.5 centimeters above the surface of the skin. For the character and distribution of the lesions Plate IX, figs. 1 and 2 may be consulted. Three tenths of a gram of the preparation was injected in the usual manner into the buttocks. Twenty days later the lesions had entirely disappeared, the skin was everywhere perfectly smooth and the ulcer on the heel entirely healed (see Plate IX, figs. 3 and 4). Since this time the patient has remained well.

Case XIV.—(Plate X.) Candido; age 10 years; duration of the disease 2 years. The lesions are situated anteriorly over the chin, left side of neck, below the left shoulder, at the bend of the left elbow, the right forearm, the left thigh, both knees, right leg and right ankle, and posteriorly over the neck, shoulders, back, buttocks and right leg. The lesions consist of patches, round or irregular in outline, sharply circumscribed, some as small as 3 millimeters, but generally 4 or 5 centimeters in diameter. They are usually covered with yellow crusts, although in some instances they show reddened summits. They are usually raised about 0.5 centimeter above the surrounding surface of the skin. There are many pigmented spots on the anterior surface of the thighs, which are evidently the result of healed lesions. (For the distribution and character of the lesions see Plate X, figs. 1 and 2.) The patient was given 0.3 gram of the preparation in the usual manner. When seen twenty days later, the lesions had entirely disappeared, the skin was everywhere entirely smooth, only pigmented patches remained where the lesions had previously existed (see Plate X, figs. 3 and 4). He since has remained well.

Case XV.—(Plate XI.) Nicomedes; age 8 years. The lesions are situated over the left eyebrow, chin, about the left shoulder, the arms, bends of the elbows, left forearm, knees, legs, left ankle, and posteriorly over the buttocks, gluteal fold, thighs and legs. There is a superficial ulcer measuring about 4 centimeters in diameter over the right heel. The lesions consist of granulomatous tumors measuring about 3 millimeters to 3 centimeters in diameter. They are sharply circumscribed, and raised about 4 or 5 millimeters above the surrounding skin. Many of them are covered with yellow crusts. Some of the smaller lesions appear as reddened papules, others as mushroom-like granulomatous masses. For their distribution and character see Plate XI, figs. 1 and 2. The patient was given 0.3 gram of the preparation in the usual manner. Twenty days afterwards the lesions had practically entirely disappeared (see Plate XI, figs. 3 and 4). He since has been well with the exception of having contracted a severe case of scabies, in some of the lesions of which *Sarcoptus scabei* was found. No urticarial eruption followed the injection.

Case XVI.—(Plate XII.) Felix; age 12 years; duration of the disease 8 years (?). The lesions are situated anteriorly over the chin, neck, left axilla, on the right arm, below the right axilla, the bends of the elbows, above the knees, the left foot, over the fourth and little toe, and posteriorly over the neck, shoulders, back, elbows, forearms, buttocks, above the popliteal spaces, legs and right ankle. The lesions consist of papillary granulomatous tumors varying from 4 millimeters to 3 centimeters in diameter, round or irregular in outline, and raised about 5 millimeters above the surrounding skin. They are usually covered with yellow crusts, or when not so covered they are red in color. Small blood vessels may be seen traversing these as a net work. Numerous pigmented spots are present over the knees, legs, ankles and buttocks, the result of older lesions. On the fourth toe of the left foot there is an ulcerating granulomatous lesion. For the distribution and character of the lesions see Plate XII, figs. 1 and 2. The patient was given 0.3 gram of the preparation in the usual manner. Twenty days later the lesions had entirely healed, the skin was everywhere smooth, only very slightly reddened areas of skin remained where they had previously existed (see Plate XII, figs. 3 and 4). The patient since has remained entirely well.

Case XVII.—Esteban; age 12 years; duration of the disease one year. The lesions consist of papillary granulomata situated anteriorly over the shoulders, bend of the left elbow, and posteriorly over the left elbow. They measure about 2 to 3 centimeters in diameter, and are raised above the surrounding tissue. Over the right heel is a partially ulcerated granulomatous lesion measuring about 3 centimeters in diameter. There are numerous scars over the chest, which are the result of old lesions. The patient was given 0.3 of a gram of the preparation in the usual manner. When seen twenty days after the injection the lesions had entirely disappeared, and the skin was everywhere entirely smooth. He since has remained well.

Case XVIII.—Juan; age 8 years; duration of disease 4 months. There is an ulcerating granuloma measuring about 3 centimeters in diameter situated over the anterior surface of the right leg. Over the left leg, posteriorly, there are five granulomatous lesions measuring 5 millimeters to 1 centimeter in diameter, covered by yellow crusts. There are numerous scars over both legs which are the result of earlier lesions. The patient was given 0.3 gram of the preparation in the usual manner. Twenty days later all signs of the lesions had disappeared, the skin was entirely smooth. He since has remained well.

Case XIX.—(Plate XIII.) Francisco; age 24 years; duration of the disease 7 months. He is unmarried, and has never had syphilis. No scar on the penis. The lesions are situated anteriorly over the neck, shoulders, chest, abdomen, arms, forearms, and thighs, and posteriorly over the neck, shoulders, back, arms, buttocks and legs. The lesions consist of numerous small pappillomata measuring from 2 to 4 millimeters in diameter, sharply circumscribed, and raised from 3 to 4 millimeters above the surrounding skin. Some of the larger ones are covered with yellow crusts. For distribution and character of the lesions see Plate XIII, figures 1 and 2. The patient was given 0.4 gram of the preparation in the usual manner. Fifteen days after the inoculation the skin was perfectly clear and smooth (see Plate XIII, figures 3 and 4). He since has remained well.

Case XX.—Tiburcio; age 10 years; duration of the disease is stated to be one month. Evidently yaws has been present for a longer time. The lesions are situated anteriorly over the right chest, below the clavicle, left breast below the nipple, both forearms, scrotum, left thigh, above the right knee, and posteriorly over the forearms, left buttock, both thighs, legs, and left ankle. The lesions consist of granulomatous tumors measuring usually about 1 to 3 centimeters in diameter, sharply circumscribed, round or irregular in outline, and raised for a distance of about 4 or 5 millimeters above the surrounding skin. Many of them are covered with yellow crusts; in the case of others they are red in color and the surface uneven. The patient was given 0.3 gram of the preparation in the usual manner. After twenty days the skin was entirely clear and smooth. He since has remained well.

Case XXI.—Maximo; age 5 years; duration of the disease 5½ months. The lesions are situated about the mouth, on the upper and lower lips, on the chin and neck, in the left axilla and on the posterior surface of the scrotum. They consist of granulomatous tumors measuring from 6 to 10 millimeters in diameter, and raised from 3 to 5 millimeters above the surrounding skin. The patient was given 0.25 gram of the preparation in the usual manner. After nine days the lesions had completely disappeared and the skin was perfectly smooth. He since has remained well.

Case XXII.—Ling (Chinaman); age 35 years. The lesions consist of five granulomata measuring from 1 to 1.5 centimeters in diameter, situated on the left leg and above the left knee. There is also an ulcerating granuloma measuring about 2 centimeters in diameter on the left ankle. A smear from one of these granulomata shows numerous spirochætæ. The patient was given 0.45 gram of the preparation in the buttocks. After three weeks the granulomatous lesions had entirely disappeared and the ulcer entirely healed. He since has remained well.

Case XXIII.—Pedro; age 18 years; duration of the disease 4 months. The lesions are situated anteriorly over the forehead, cheeks and chin, the chest, shoulders, arms, and forearms, thighs and legs; posteriorly over the shoulders, arms, chest, and legs. They consist of papules measuring from about 3 to 6 millimeters in diameter and raised for a distance of 3 to 4 millimeters above the surrounding skin. A few are covered with yellow crusts. The patient was given an injection of 0.4 gram of the preparation. After 18 days the skin was perfectly smooth, and only dark pigmented spots remained where the papules had formerly existed. He since has remained well.

Case XXIV.—Pablo; age 14 years; duration of the disease 2½ years. The patient has been treated at St. Luke's Dispensary for 1½ years. The condition was formerly diagnosed "fungus foot." At St. Luke's Dispensary he has treated with mercury and iodides internally, and locally with mercurial ointment, bichloride of mercury, lysol, Peru balsam, silver nitrate and permanganate of potash dressings. The lesions were also cauterized and curetted on several occasions. Very slight improvement followed all of this treatment. When seen by the author the lesions were confined to the right foot and ankle. Above the external malleolus there were four ulcerating granulomata measuring from 1 to 1.5 centimeter in diameter. Over the dorsum of the foot there was a large ulcerating granulomatous mass measuring about 6 centimeters in diameter. The greater part of the sole of the foot was also occupied by a larger ulcerating mass, the margins of which were very irregular in outline. Spirochætæ were found in several smears from the ulcerating granulomata. A diagnosis of tertiary yaws was made, and the patient was injected with 0.35 gram of the preparation in the usual manner. Before this treatment he had complained of much pain in the foot. Six days after the injection he stated that the pain had entirely disappeared. He was seen occasionally by his physician during the next two weeks who reported that a very great improvement had taken place in the condition of the foot, and that the lesions were rapidly healing. He was not seen by the author until 1½ months after the injection. At this time the lesions which existed formerly had entirely disappeared. Where the ulcer and granulomata formerly had been present, only firmly contracted scar tissue remained. Above the external maleolus patches of pigmented skin were present. The patient since has remained entirely well.

Case XXV.—(Plate XIV.) Juan, age 16. Duration of the diseases 3 weeks, during which time he has been treated with Chinese medicine containing iodides but with no favorable result. Denies syphilis. No sore or scar on penis. The lesions are situated on the forehead, cheeks, nose, upper lip, chin, neck, chest, abdomen, scrotum, shoulders, arms, forearms, palms of hands, thighs, knees, legs, ankles and feet; and posteriorly over the neck, shoulders, back, arms, elbows, forearms, buttocks, legs and ankles. The distribution is almost universal, although the lesions are more marked on the face and upper portion of the trunk. They consist of papules measuring from about 3 millimeters to one centimeter in diameter; the largest are situated on the face. They are sharply circumscribed, the largest ones raised for a distance of 3 to 4, the smallest for a distance of 1 to 2 millimeters above the surface of the surrounding skin. On the face and on many parts of the chest the papillary tumors are covered with yellow crusts. Elsewhere the papules are slightly reddened, with dry surfaces. Smears from the papules show numerous spirochætæ. For the character and distribution of the lesions see Plate XIV.

The patient was given an injection of 0.38 gram of the preparation in the buttocks in the usual way. The spirochætæ had disappeared from the lesions three days later. The lesions gradually disappeared; after twenty days the skin was clear, as may be seen by Plate XIV. The patient since has remained well.

CONCLUSION.

Dioxy-diamido-arsenobenzol appears to be an ideal specific for yaws. Three or four days after the injection of the drug, the granulomatous lesions begin to disappear and in the course of from ten to twenty days they usually have disappeared entirely leaving a perfectly smooth, pigmented skin where the lesions previously existed. The absorption of tumor masses measuring several centimeters in diameter and about a centimeter in thickness in so short a time, and under the influence of no local treatment whatever, has been very striking and surprising. Indeed, in the severe cases the disappearance of the lesions and the cures produced could be most aptly spoken of as marvelous. Even in cases where large granulomatous masses or deep ulcerations existed, these were healed within from two to four weeks. I do not know of any more striking example in medicine of a specific action than of that produced by dioxy-diamido-arsenobenzol on the lesions of yaws.

A slight reddening appears about the margins of the lesions in from twenty-four to forty-eight hours after the injection of the preparation. The center of the lesion then usually assumes a purplish or bluish, congested appearance. Phagocytes are attracted to this area which now assumes a grayish or brownish hue. The spirochætæ quickly disappear and the granulomatous tissue becomes absorbed, leaving dark, pigmented areas of skin which later resume their normal color. In the cases where crusts have existed, these frequently are not absorbed, but drop off.

As stated above, none of the cases have shown any signs of relapse, although they received but a single injection, and over four months have elapsed since most of them were inoculated.

Nevertheless, I believe that in a few of the most severe instances of the disease, where the ulcerations are extensive and of long standing, a second inoculation given about three weeks after the first one may be advisable. In a case of syphilis in a European who had been treated with mercury and iodides, according to his statements, for two years, in which the testicle was swollen to a diameter of about 15 centimeters and a large ulcer measuring about 10 centimeters in diameter was situated on the scrotum, 0.4 gram of dioxy-diamido-arsenobenzol was given by injection into the buttocks. A very rapid diminution in the size of the testicle and of the ulcer occurred during the following three weeks, but the ulcer did not entirely heal nor did the testicle reach its normal size until a second intravenous injection of 0.4 gram of the drug was given. Then apparently a perfectly normal condition was brought about. Only in Number IV of the yaws cases which I treated with this preparation was there any question as to whether a second dose should have been given and as to whether a second one might not have hastened the cure.

However, the lesions eventually entirely healed as a result of the primary injection. The dose of the preparation for the treatment of yaws should be from 0.25 to 0.3 gram for children and from 0.4 to 0.5 gram for adults. Smaller amounts may not give such favorable results.

Some observers believe that it is not advisable to attempt to repress the eruption of yaws, as this may be accompanied by considerable constitutional disturbance. The employment of dioxy-diamido-arsenobenzol simply caused the eruption to fade away. There were no unfavorable constitutional symptoms other than an occasional transitory rise of temperature produced thereby, and the patients seemed improved in health following the disappearance of the eruption.

A number of authors have also laid great stress upon the local treatment of the disease. If dioxy-diamido-arsenobenzol is employed, the local treatment is entirely unnecessary, except in cases of severe ulceration and where organisms other than *Treponema pertenuis* have invaded the lesions. Case IV would undoubtedly have been cured more quickly if the ulcerating granulomatous masses had been curetted, disinfected, and dressed daily with sublimate solutions, since spirochætæ other than *Spirochaeta pertenuis* and bacilli and cocci were present in the lesions. However, even in this case they eventually entirely healed without local treatment.

The cure of yaws by this preparation, and the successful results which have been obtained with it in the treatment of certain cases of syphilis, may suggest again the identity of yaws and syphilis. It does not appear strange that this preparation should have such a destructive action against both *Treponema pertenuis* and *Treponema pallidum,* since both from a morphologic and biologic standpoint these two organisms appear closely related. Indeed, potassium iodide, which is so valuable in the treatment of syphilis, has hitherto been the most successful remedy employed in the treatment of yaws. As has been pointed out by other observers, the therapeutic argument for the identity of yaws and syphilis and hence for the identity of their specific organisms, is very fallacious. Many instances in medicine might be quoted in support of this statement. Quinine which destroys certain forms of *Plasmodium malariæ, Plasmodium vivax,* and *Laverania malariæ,* also destroys *Amœba dysenteriæ.*

In conclusion it would appear that dioxy-diamido-arsenobenzol is as important a specific for yaws as quinine is for malaria. Therefore, a fourth medicinal specific in medicine has been discovered.

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ILLUSTRATIONS.

PLATE I. Case I before treatment.

II. Case I twelve days after treatment. The skin is everywhere perfectly smooth. In the photograph of the posterior view it appears that tumors still exist in the region of the popliteal spaces. This appearance is due to the areas of pigmented skin. The granulomata here as elsewhere have entirely disappeared and the skin is entirely smooth.

III. Case II before treatment.

IV. Case II nine days after treatment. The skin is everywhere smooth. Pigmented patches are visible on the lower extremities both anteriorly and posteriorly.

V. Case III before treatment.

VI. Case III fourteen days after treatment.

VII. Case IV before treatment.

VIII. Case IV after treatment.

Fig. 1. Nine days after treatment. The lesion on the chin is not entirely healed. At the bends of the elbows the character of the lesions has entirely changed. The formation of scar tissue is evident.

Figs. 2 and 3. Three weeks after treatment. There are scabs over the bend of the left elbow anteriorly, and posteriorly over the right elbow and popliteal spaces. These have since disappeared and the skin has become smooth.

IX. Case XIII.

Figs. 1 and 2. Before treatment.

Figs. 3 and 4. Twenty days after treatment. The skin is entirely smooth.

X. Case XIV.

Figs. 1 and 2. Before treatment.

Figs. 3 and 4. Twenty days after treatment.

XI. Case XV.

Figs. 1 and 2. Before treatment.

Figs. 3 and 4. Twenty days after treatment.

XII. Case XVI.

Figs. 1 and 2. Before treatment.

Figs. 3 and 4. Twenty days after treatment.

XIII. Case XIX.

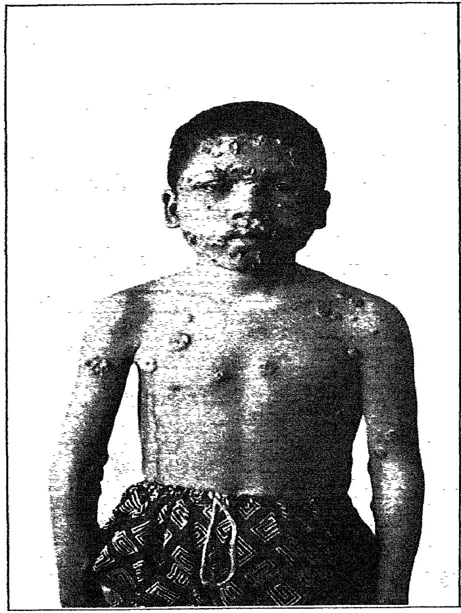
Figs. 1 and 2. Before treatment.

Figs. 3 and 4. Twenty days after treatment.

XIV. Case XXV.

Figs. 1 and 2. Before treatment.

Figs. 3 and 4. Twenty days after treatment.



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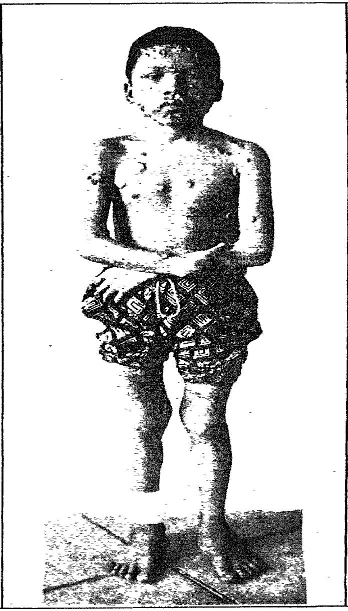

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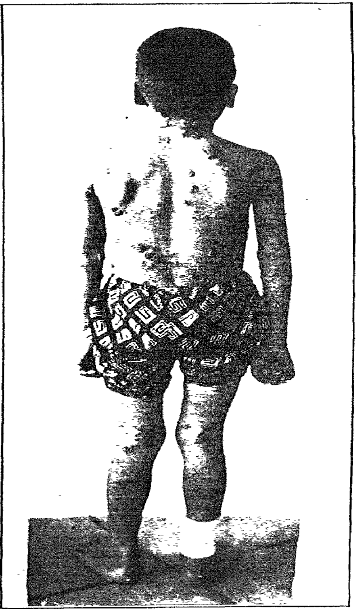

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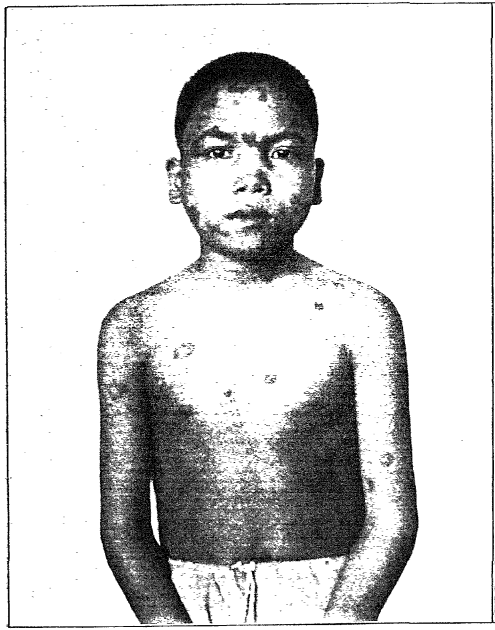

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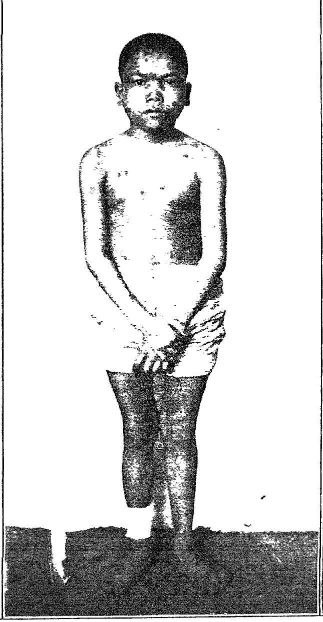

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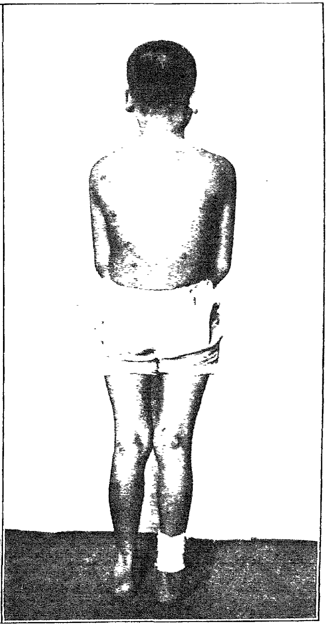

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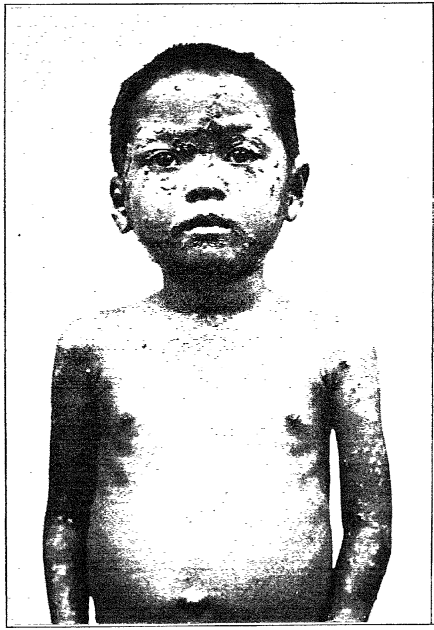

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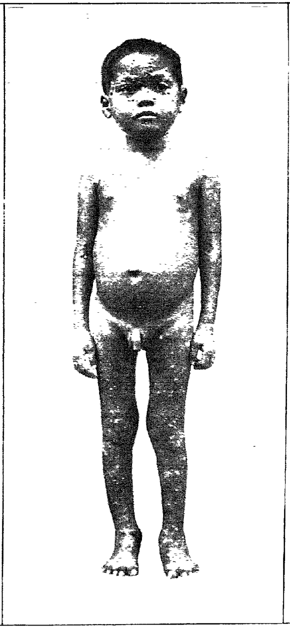

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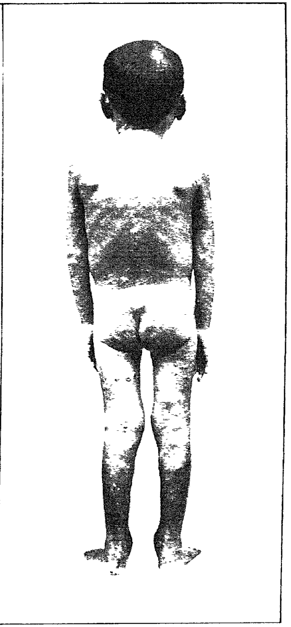

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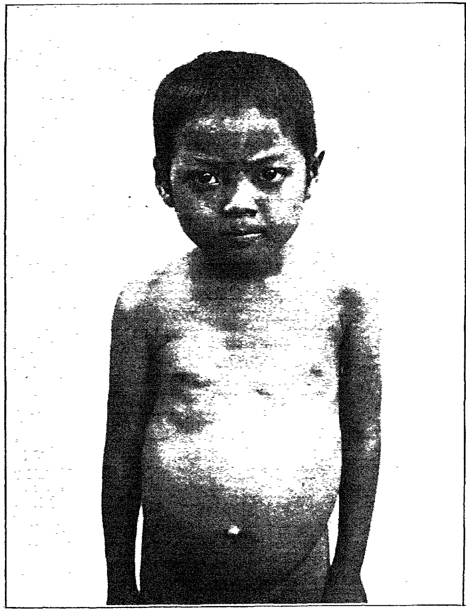

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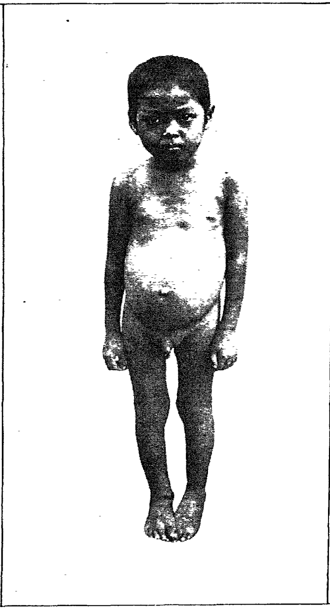

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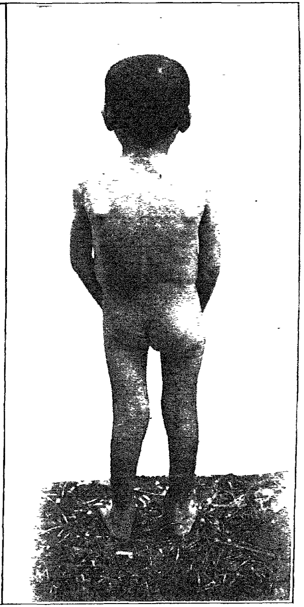

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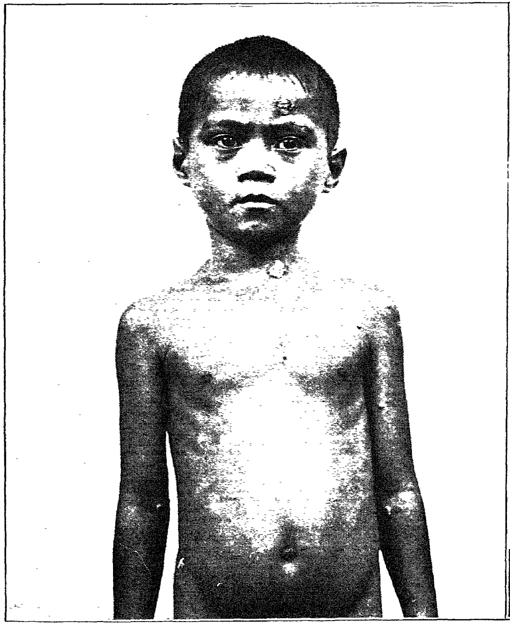

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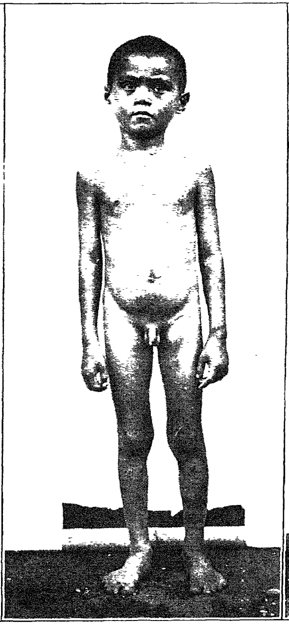

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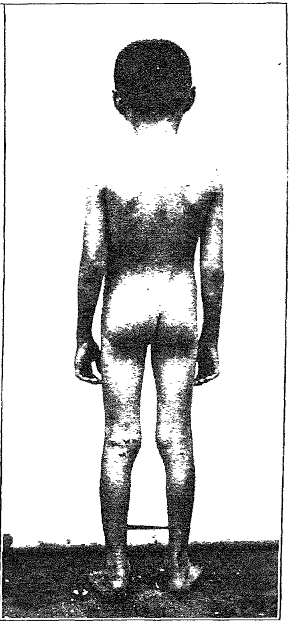

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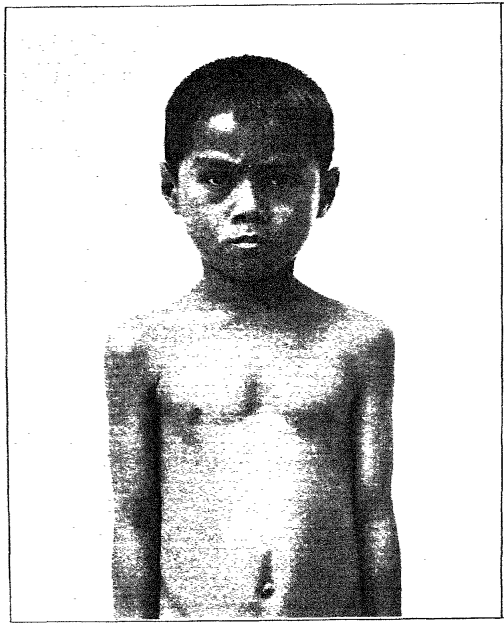

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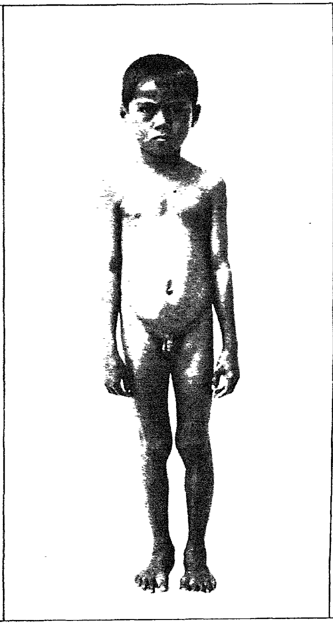

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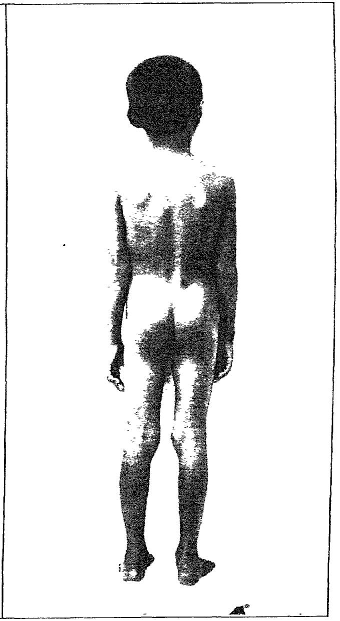

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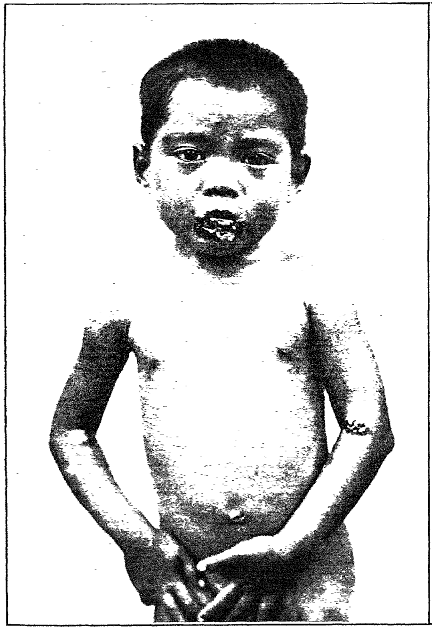

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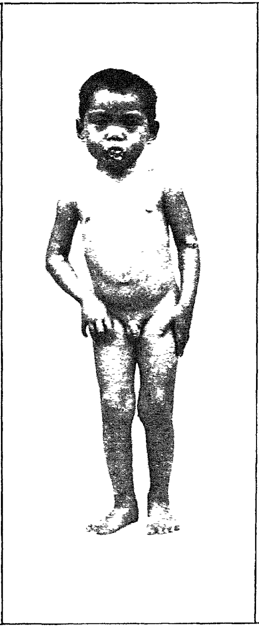

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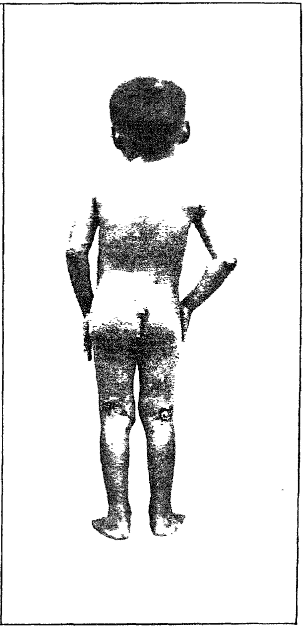

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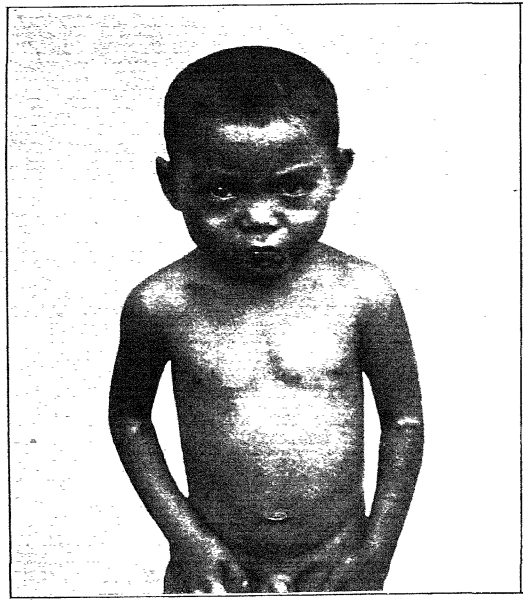

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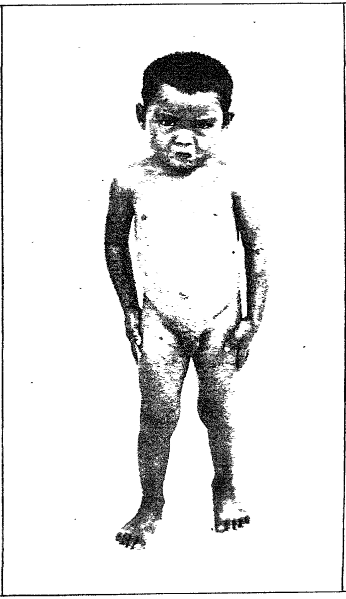

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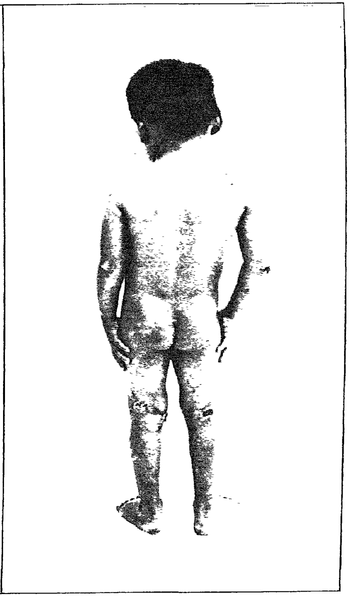

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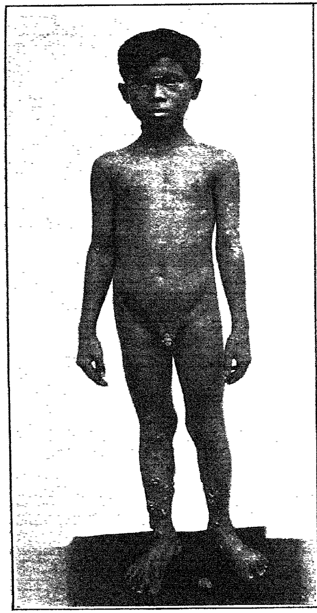

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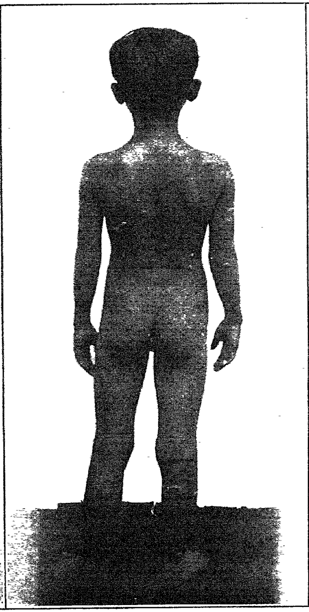

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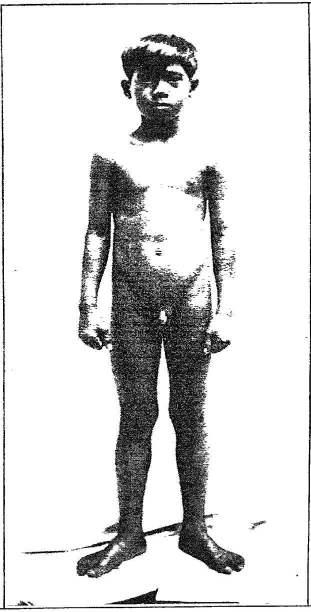

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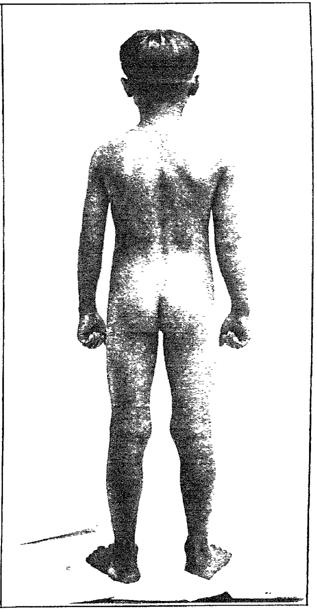

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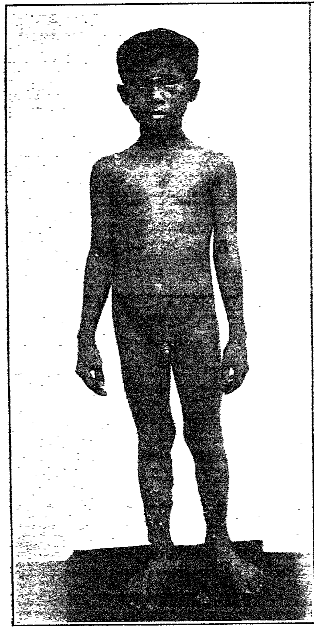

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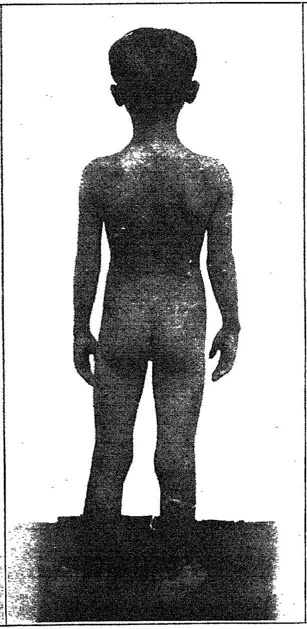

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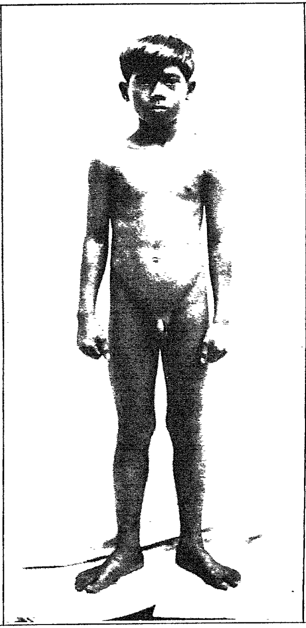

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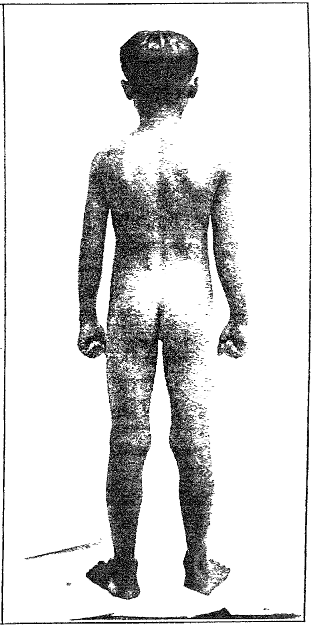

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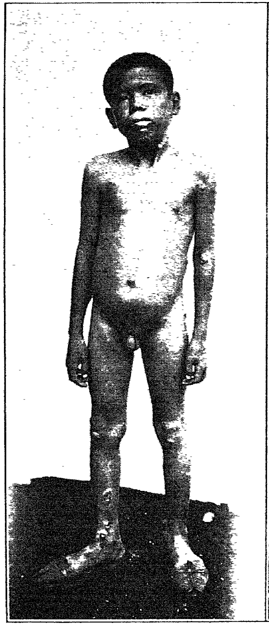

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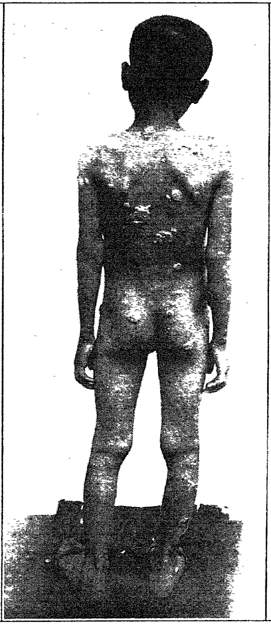

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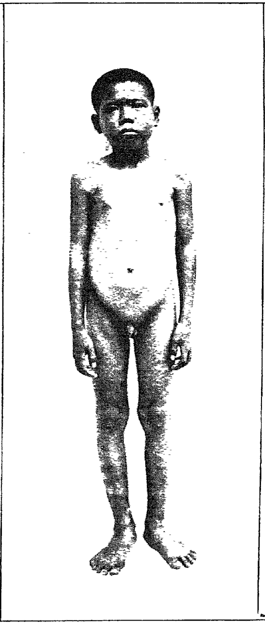

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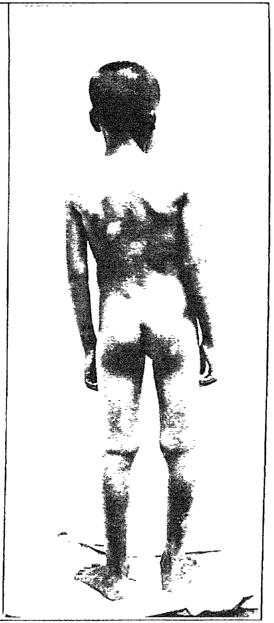

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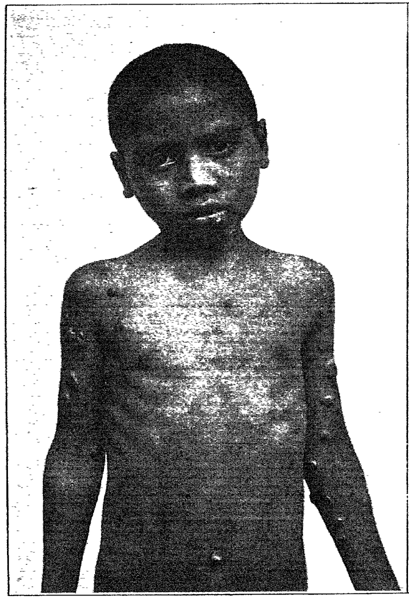

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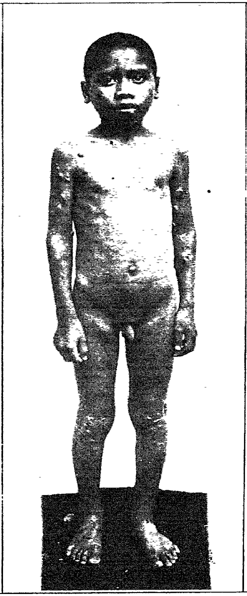

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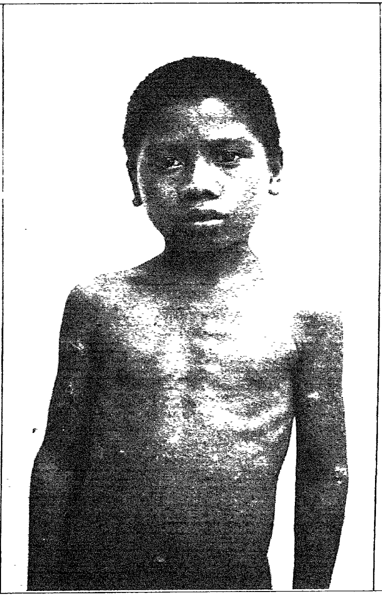

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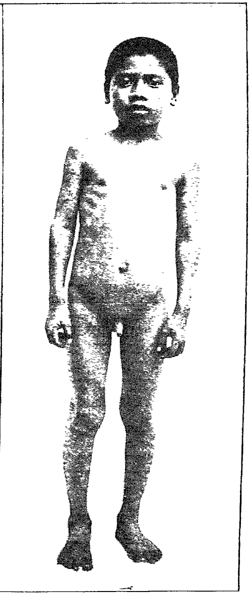

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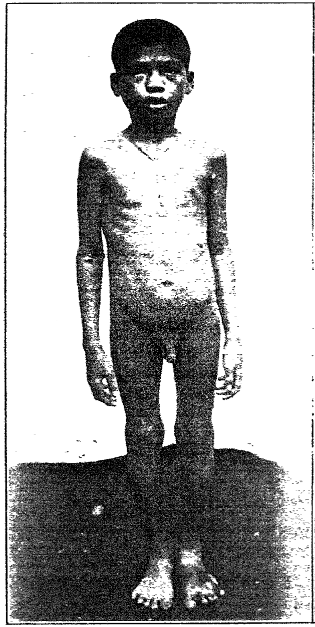

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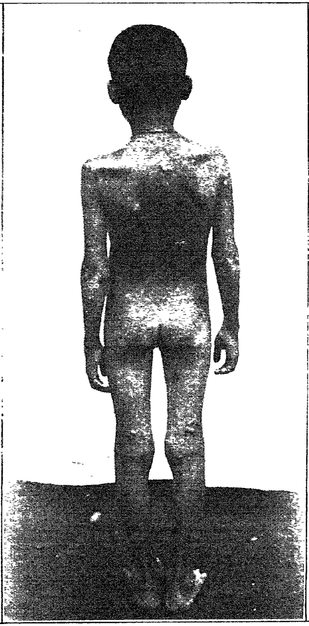

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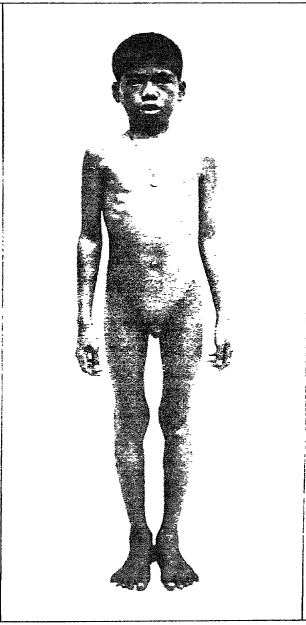

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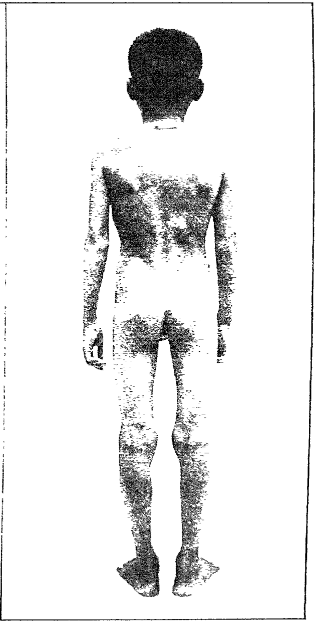

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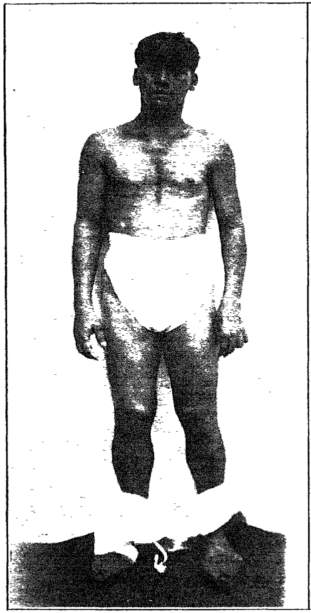

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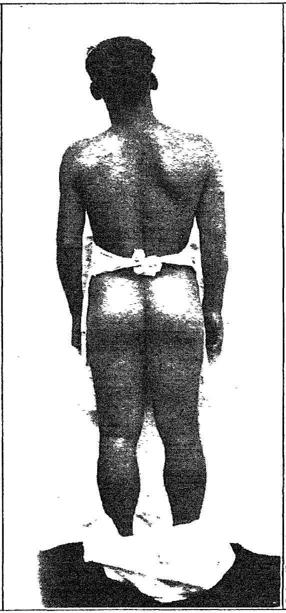

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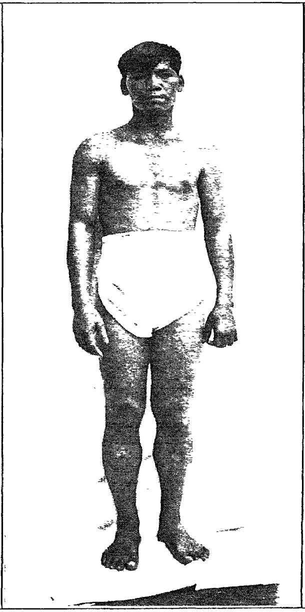

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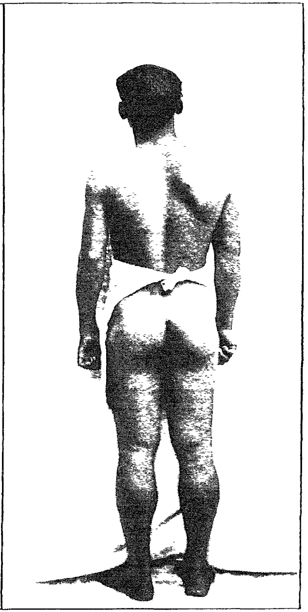

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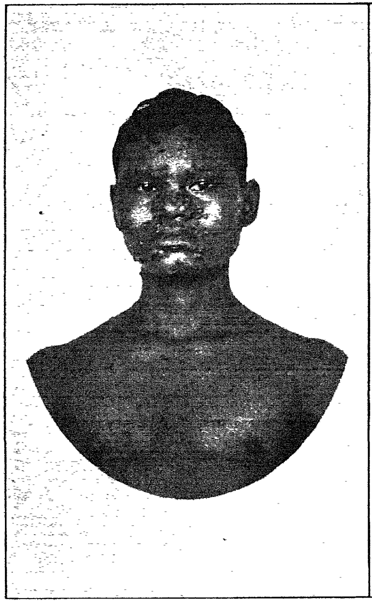

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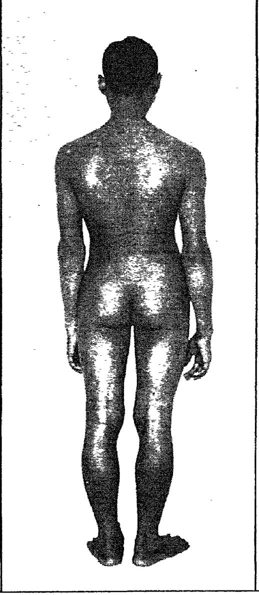

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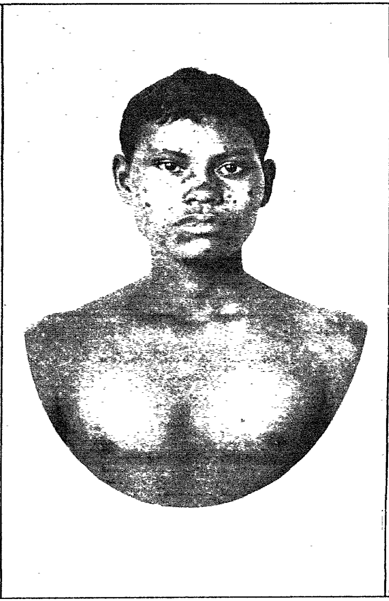

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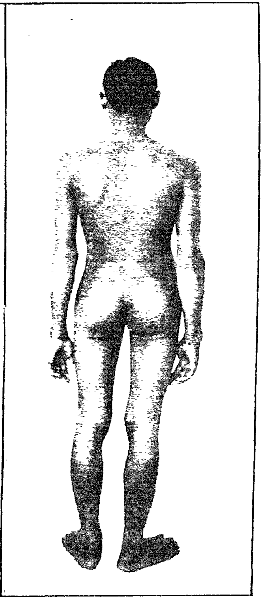

FIG. 4.

PLATE XIV.

REVIEWS.

A Textbook of Experimental Physiology For Students of Medicine. By N. H. Alcock, M. D., D. Sc., and F. O'B. Ellison, M. D. Cloth. Pp. xii+139, 36 illustrations. Price $1.50 net. Philadelphia: P. Blakiston's Sons, 1909.

This book, with a preface by Ernest H. Starling, gives a clear description of the experiments which should be performed by medical students in the physiological laboratory. Not only are the usual muscle and nerve experiments included, but also the more important ones on mammals. The idea of the authors is not simply to show the student *how to experiment,* but rather to teach him *how to observe.* The physiologic anatomy of the rabbit is an especially excellent example of this method of instruction. Some experiments, such as the demonstration of the action of secretin on pancreatic secretion, or the analysis of the gases of the blood by Haldane's apparatus, seem to the reviewer to be somewhat difficult for an elementary course. Certain procedures are inserted to comply with the restrictions which are placed by law upon vivisection in Great Britian.

Hans Aron.

Examination of the Urine. A Manual For Students and Practitioners. By G. A. DeSantos Saxe, M. D. 2d ed. Cloth. Pp. 448. Price $1.75. With text illustrations and colored plates. Philadelphia and London: W. B. Saunders Company, 1909.

Modern clinical medicine demands a certain amount of laboratory work from nearly all practitioners and this book is destined as a guide for such clinical examination of urines. The first part, "Chemic Examination of the Urine," is hardly more than a careful compilation of what is found in a great number of other text and hand books. The second part, "Microscopic Examination," especially the chapters on "Urinary Diagnosis" and "Functional Renal Diagnosis," probably never has been treated so clearly and thoroughly. The author gives here a number of original pictures and many practical suggestions based on his own experience. The clinical significance and importance of the different findings are well discussed, making the book of real value for the practicing clinician.

The questions at the end of each chapter remind one very forcibly of the so-called *vade mecum* used by students not of the best type just before examination, and impress the reviewer as somewhat out of place in a work of this character.

Hans Aron.

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[OVER.]

THE PHILIPPINE

JOURNAL OF SCIENCE

B. MEDICAL SCIENCES

VOL. V NOVEMBER, 1910 No. 5

HYDROPHOBIA IN THE PHILIPPINES.

By F. W. DUDLEY[1] and E. R. WHITMORE.[2]

The question of whether rabies does or does not occur either among the lower animals or man in the Philippines has been unanswered for a long time, and, while a number of medical men have been convinced that rabies is present in this Archipelago and considerable clinical evidence in favor of that belief has been collected, still several attempts to demonstrate scientifically its occurrence have failed; furthermore, several trials having for their end the keeping alive of a strain of "fixed virus" imported from Japan, have been unsuccessful, the virus either did not kill rabbits in Manila at all, or ceased to do so very soon after its importation. The question therefore arose as to whether the virus of rabies could continue in a viable condition in this locality.

One of us, as the result of an extensive clinical experience in these Islands, became firmly convinced that rabies does occur here, and read a paper on "The Prevalence of Hydrophobia in the Philippine Islands" at the meeting of the Philippine Islands Medical Association, February 28, 1907.[3] Up to that time Dudley had collected statistics of 158 deaths from hydrophobia in the human, and since then has received additional reports of 244 deaths, making a total of 402 reported human deaths from hydrophobia in the Philippines since about October 1, 1902. Thirty-one of the thirty-nine provinces in the Philippines, to which must be added the Island of Mindanao (Moro Province) and the district of Manila, have reported deaths from hydrophobia. Many of these reports so accurately describe rabies that they can hardly refer to any other disease.

---

[1] Attending surgeon, St. Paul's Hospital, Manila.

[2] Major, Medical Corps, United States Army, detailed for civil duty to the Biological Laboratory, Bureau of Science. The laboratory work was done at the Biological Laboratory, Bureau of Science.

[3] Dudley, F. W. *Jour. Amer. Med. Asso.* (1908), 51, 2143.

However, none of these cases had been proved to be rabies. Accordingly, we decided to take up the study of the problem and determine, if possible, whether rabies actually does exist in this Archipelago. On April 1, 1910, we mailed a circular letter to all the physicians in the Philippines, asking them to send us the heads or brains of animals killed for, or dead of, suspected rabies; the material to be sent packed in ice, or in 50 per cent glycerine where ice was not available. We requested also that they report any cases of human rabies to us, so that if possible we might see the patients.

In response to this circular, Dr. Salvador Gomez, of Angeles, Pampanga Province, sent us the bodies of two dogs on April 16, 1910. These two animals had been bitten by a suspected rabid dog on March 22, and their owner, recognizing the danger of rabies, kept them tied from that date.[4]

One of these dogs became sick on April 10, the other on April 14. They refused to eat, saliva dribbled from their mouths, and they showed a tendency to snap and bite at everything. One of them escaped one day, and after running about bit two other dogs and a pig. On the following day another of the dogs escaped and attacked its mate, and the two animals fought viciously. The owner then killed both in the way usual among the natives, namely, by striking them over the head with a club. A few hours afterwards Doctor Gomez learned of the incident, secured the bodies and sent them to us.

The animals had been dead about forty-eight hours when we received them and no ice had been available for packing them for shipment. The skull of one (number 2) had been crushed by the blow that killed it, and the brain cavity was filled with a mass of blood clots, brain tissue, and bone fragments. We succeeded in demonstrating Negri bodies in the brain tissue of both of these animals; in the hippocampus and cerebral cortex of dog number 1 and in a piece of the cerebellum of dog number 2. The bodies stained rather faintly and it was difficult to bring out the "inner bodies" because of the length of time which had elapsed since the death of the animals and the beginning of putrefaction of the brain tissue.

---

[4] The natives throughout the Islands understand that a dog bitten by another is likely to die, and that a person bitten by such a dog will probably die. So, when a dog is bitten it is always killed or tied up.

An emulsion of the brain tissue from each dog was injected intramuscularly into five rabbits. Rats were not available for inoculation. The brain tissue of dog number 2 killed all rabbits within eighteen hours, because of the contamination which was present. All rabbits inoculated with the emulsion of brain tissue from dog number 1 died within from fifteen to twenty days with the symptoms of rabies, and we were able to demonstrate Negri bodies and Lentz passage bodies in the brains of these rabbits.[5] (See Pl. I.) This strain of virus was carried through seven passages in rabbits between April 17 and July 9, and at the end of that time it regularly killed rabbits with typical rabies in nine days when inoculated subdurally. We did not attempt to demonstrate Negri bodies or Lentz passage bodies in the brains of rabbits beyond the third passage. It was not considered necessary to carry this strain further and so no more inoculations were made, the strain being preserved in neutral glycerine in the refrigerator.

On May 29, Dr. Ambrosio Reyes invited us to see a case of human rabies under his care here in Manila.

The patient, a little boy 8 years old, while playing on April 5 with other children in a street near his home, was bitten on the left forearm by a strange dog that ran in among the children. The wounds were cauterized with carbolic acid and they healed in eight days. On May 27, vesicles were noted over the site of the bite. This herpetic eruption traveled up the forearm and arm, over the left pectoral and left scapular regions, and finally up onto, and behind, the left ear. The lesions itched intensely and the boy scratched them, leaving an abraded surface from which a thin, clear serum exuded. In the afternoon and evening of May 27, the boy became drowsy and did not care to play. The next morning there was difficulty in swallowing, and the parents, recognizing that the boy was developing rabies, called Doctor Reyes. On May 29 the boy was unable to swallow. Water taken into the mouth caused a spasm in his throat and he immediately spat the water out. There was almost complete suppression of urine. On May 30 the sight of water or food would provoke a severe spasm and the boy died in a convulsion on the evening of May 30.

The case clinically was one of typical rabies, and Doctor Reyes recognized it as such on May 28. He informed us that this is the eighth case of human rabies he had seen in a private practice of twenty years in Manila. From his early and accurate diagnosis in this case, there is every reason to believe that all of his other seven cases were rabies.

Negri bodies were not found in the brain of this boy, but an emulsion of the brain injected subdurally and intramuscularly into rabbits killed all of them with typical rabies in from fourteen to twenty days. Negri bodies and Lentz passage bodies were readily demonstrated in the brains of these rabbits. This strain was carried through three passages in rabbits between May 31 and July 18, all of the last passage rabbits dying of typical rabies in about two weeks. It was not considered necessary to carry this strain any further, so no more inoculations were made, it being preserved in neutral glycerine in the refrigerator.

---

[5] Dudley and Whitmore: Rabies in the Philippines. A Preliminary Report, read before the Manila Medical Society, May 2, 1910. *Bull. Manila Med. Soc.* (1910), 2, 99.

We had now shown so conclusively that rabies does occur in dogs in the Philippine Islands and in the human in Manila that it was necessary for us to secure a strain of fixed virus and carry it along in Manila. It did not seem advisable to wait for one of our own strains to become "fixed," as a year or more probably would be required to reach that end; and four attempts to bring in a fixed virus had already failed, the virus in each instance losing its virulence en route or else very soon after its arrival. Accordingly, one of us (Whitmore) was sent to Saigon, French Indo-China, to study the methods of the Pasteur Institute for preventive treatment of rabies and to bring back if possible a fixed virus in animals and in glycerine. The fixed virus in use at Saigon was brought out from the Paris Institute some months ago. It had gone through upward of eight hundred passages in Paris and fifteen in Saigon.

Rabbits were inoculated subdurally with fixed virus at the Saigon Institute and were placed on a boat sailing directly for Manila. At the same time fixed virus was placed in a bottle of neutral glycerine in a refrigerator on the same boat. The rabbits arrived in Manila in good condition and died of experimental rabies in the Biological Laboratory, Bureau of Science.

The fixed virus in glycerine had preserved its full virulence and when inoculated subdurally into rabbits in Manila killed them in about ten days. The brain tissue from the imported rabbits was also fully virulent when inoculated into rabbits here. This strain of fixed virus has now passed through five passages of rabbits in the Biological Laboratory, Bureau of Science, and constantly kills rabbits in about ten days, with typical symptoms of experimental rabies. This strain is being used for the protective inoculation against rabies which is now being carried on in Manila.

SUMMARY.

1. We have shown conclusively that rabies occurs among dogs in the Philippines, (*a*) by finding Negri bodies in the brain tissue of two dogs killed for suspected rabies; (*b*) by carrying the virus from the brains of one of these dogs through seven passages in rabbits, rabbits of the seventh passage dying in nine days of typical experimental rabies; (*c*) by demonstrating the presence of Negri bodies and Lentz passage bodies in the brain tissue of these rabbits up to the third passage.

2. We have shown conclusively that rabies does occur in the human in Manila, (*a*) by observing a case that was clinically typical rabies;

(*b*) by carrying the virus from the brain of that case through three passages in rabbits, the rabbits of the third passage dying of typical experimental rabies in about two weeks; (*c*) by demonstrating the presence of Negri bodies and Lentz passage bodies in the brain tissue of three rabbits up to the third passage.

3. We have succeeded in bringing a fixed virus from Saigon to Manila in animals and also in neutral glycerine in a refrigerator. The virus brought in both ways has retained its full virulence since its arrival here. By means of this work it has therefore been made possible to carry on protective inoculation against rabies in Manila.

NOTE.—Ashburn and Craig reported in the Military Surgeon, June, 1907, vol. 21, p. 529, as follows:

"*Rabies.*—On the 7th of June we obtained from the land transportation corral, quartermaster's department, Manila, the body of a dog thought to be dead of rabies. The animal had been under observation during the entire period of its illness and the symptoms and history both indicated that it was suffering from the disease mentioned. Examinations of smears from its brain, according to the method spoken of as affording 'a rapid diagnosis of rabies' showed bodies corresponding in form, size, and staining reaction with the description of Negri bodies. Cerebral inoculation of three rabbits with the same brain substance, however, has failed to induce in any one of them any symptoms of rabies or of other disease."

In their quarterly report ending September 30, 1907, to the Surgeon-General, United States Army, they further state:

"In our last quarterly report we recorded some observations on the examination of the brain of a supposedly rabid dog. The brain showed bodies indistinguishable from 'Negri bodies' and, as intracerebral inoculation of four rabbits had not induced the disease in them after a period of twenty-three days, we concluded that the bodies were probably not Negri bodies, or, if so, that they were not necessarily indicative of rabies. Since that time, however, all four rabbits have died of the disease, and, by the passage through other animals, Doctor Ohno has somewhat increased the strength of the virus and lowered the period of incubation.

"Our observations in this one case, therefore, go to emphasize the diagnostic value of the Negri bodies, rather than to belittle it."

It will be noted that the dates on which the rabbits were taken ill and died are not given. Nothing is said about the microscopical examination of the brains of these rabbits. In any event the rabbits died some time after the twenty-third day and for this reason alone Ashburn and Craig were in all probability not dealing with true rabies. In the work here all of our rabbits developed the disease between the twelfth and seventeenth day (most of them on the fifteenth day). None died later than the twentieth day. If Ashburn and Craig had been dealing with rabies, some of their rabbits would certainly have shown illness before the twenty-third day.

Doctor Ohno in a report to the Director of the Bureau of Science, dated July 9, 1907, evidently referring to these same experiments (however, only accounting for three of the four rabbits), states that three rabbits were inoculated on June 8. One developed "slightly typical symptoms" on June 29, twenty-one days after inoculation. He does not state whether this rabbit died or was killed. The second rabbit developed "slight symptoms" on June 30 (twenty-two days after inoculation) and was killed by chloroform on July 1. The third rabbit is recorded in his table as having succumbed July 9, thirty-one days after inoculation. It is not stated whether it died or was killed by Doctor Ohno. It will be noted, Ashburn and Craig stated that these rabbits died after the twenty-third day. Nothing is said about the microscopical examination of the rabbits' brains for Negri bodies. This report serves to confirm the opinion expressed in the foregoing.*

F. W. DUDLEY.

---

* The report made by Doctor Ohno was received in the absence of the Chief of the Biological Laboratory and is printed at the end of this number. (Ed.)

ILLUSTRATION.

EXPLANATION OF PLATE I.

Section through hippocampus of rabbit which died twenty days after intramuscular inoculation of emulsion of brain of dog number 1. Stained with eosin-methylene blue, according to Lentz's method B. Zeiss: Compens.-ocular 12, obj. apochromat. 2 mm homog. Immers. N. A. 1.30, Tube length 160 mm.

The nerve cell to the right at the top shows marked degeneration. The nucleus stains a dull violet and is not marked off from the cell protoplasm, while the nucleolus stains deeper blue than in the other nerve cells. The "body" in the upper part of the cell stains faintly and has four rather large "inner bodies," while one "inner body" in the lower "body" is unusually large. These bodies are probably closely related to the Lentz passage bodies.

The Negri body in the cell on the left of the plate lies on top of the nucleus.

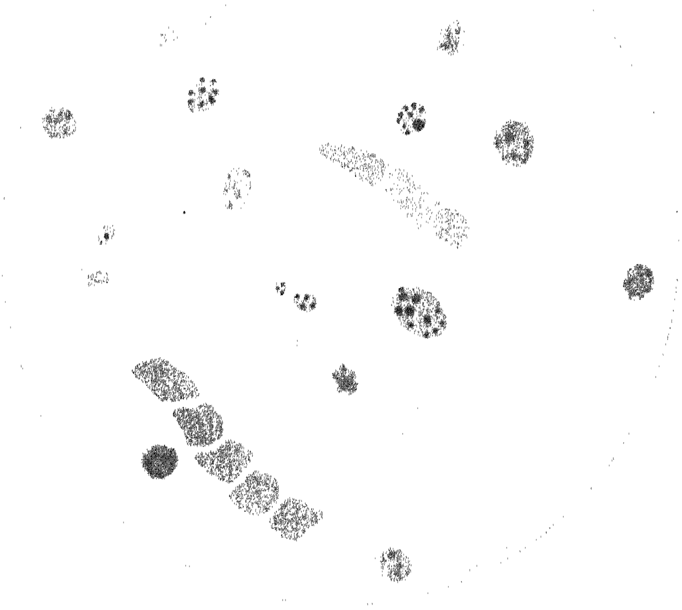

PLATE I.

RESEARCHES ON ACARIDS AMONG LEPERS.

By M. LEFEBVRE.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

M. Borrel in 1909 published two very interesting papers, "Acariens et Cancers" and "Acariens et Lèpre,"[1] in which he proposed the hypothesis based on noteworthy observations, that the agent of propagation of both these diseases might be an acarian parasite, namely, *Demodex folliculorum* Simon.

I have taken up the critical examination of this hypothesis so far as it concerns leprosy. The materials for the present investigation have been taken from lepers of the San Lazaro Hospital in Manila. The following methods principally were employed in their collection and study.

1. *Contents of the sebaceous glands collected in vivo.*—To extract the contents of the sebaceous glands, I usually made use of glass tubes, one end of which I reduced to a filament having an interior diameter of 2 millimeters. By properly pressing this open end on the skin so that it circumscribed the opening of a sebaceous gland, the entire product of the gland was forced up into the tube, and the contents of the latter then pushed by a straw onto a microscopical slide. The individuals of Demodex, if there are any, are by this means almost certain to be extracted, for they are always found at the bottom of the sebaceous cavities.

There is a chance of at least one error in the microscopic examination of this substance, for it often happens that in the mass of sebum there occur small, molded portions which so closely resemble the body of Demodex that it is nearly impossible to distinguish them from it, and all the more so because the granulations and the greasy consistency of the mass make it indistinct. Hence it is necessary to clear the preparation by a solvent. After various trials with ether, alcohol-ether, chloroform, potassium hydroxide, potassium carbonate, borax, etc., I decided on a solution of borax; the greasy substance disappeared by its use and it was easy to recognize the bodies which remained after the treatment.

2. *Cutaneous nodules excised from living lepers.*—Nodules not yet ulcerated must be chosen. The ablation is often almost painless, as many of them are anæsthetic.

3. *Pieces taken at autopsy.*—The lobes of the ear; sides of the nose; pieces of skin cut off around the various nodules; portions of the characteristic moniliform nerves, and internal organs, the spleen in particular, were used in order to compare the bacilli found therein with those observed in the skin.

---

[1] *Ann. Inst. Past.* (1909), 23, 100, 127.

I employed Borrel's fixative, the formula of which is given below, for the small pieces of tissue taken either from the living or dead body:[2]

	Grams.
Water	350
Osmic acid	2
Chromic acid	3
Platinum chloride	2
Glacial acetic acid	20

However, I prefer Meyer's acetic acid sublimate solution which consists of a saturated solution of bichloride of mercury, 100 cubic centimeters, and acetic acid, 0.5 cubic centimeter. This solution fixes well and interferes less with the staining of the sections.

The sections were for the most part either stained by the Ziehl-Neelsen method, or with eosin and crystal violet and Gram's iodine solution. This second process is the best for the study of the bacilli.[3]

I.

The first important question to decide was what percentage of both leprous and healthy individuals in Manila harbored Demodex. A research of this character among healthy people has been attempted elsewhere by several investigators. I have not had the means of doing so under favorable conditions in Manila. I might have tried, it is true, in a hospital, but the results would not have been above criticism, for all parasitologists know the great influence of the morbid state on the number of organisms living even in organs untouched by disease; and in the case in question it is particularly necessary to keep in mind that lymphatic, scrofulous, arthritic and many other affections also modify the quantity of the sebaceous matter, in which *Demodex folliculorum* lives.[4]

The results regarding the prevalence of Demodex published by different authors vary exceedingly. Gruby[5] says he found *Demodex folliculorum* in the sebaceous glands of 40 among 60 persons he examined. Moniez, and also Raillet,[6] considers this a greatly exaggerated number. Mégnin,[7] according to researches made on a regiment of artillery composed of men from all parts of France, gives an average of 1 out of every 10 individuals having Demodex. Borrel examined 20 individuals of different ages between 20 and 70 years and estimated the average at 50 per cent; it is to be noted that the subjects of this last research were hospital patients. Borrel also examined a large number of cases of epithelioma and found the percentage infected to be increased. I shall refer below to his researches on lepers.

---

[2] Acariens et Cancers. *Ann. Inst. Past.* (1909), 23, 100.

[3] Baumgarten's process, recommended for differentiating the bacillus of Hansen from that of Koch, sometimes gives misleading results. I have found, as several observers have already noticed, that tubercle-bacilli as well as the bacilli of leprosy are often stained by this process.

[4] Berlioz. Man. prat. des maladies de la peau. 3 ed. (1894), 160.

[5] *Compt. rend. Acad. Sc.* Paris (1845), 20, 569.

[6] *Zool. Med.* (1895), 635.

[7] Parasites et maladies parasitaires (1880), 272.

My personal investigations, although not conducted systematically enough to furnish a very definite conclusion, indicate that, exclusive of children, Demodex does not live on more than one-quarter of the individuals who are in health.

I believe that the apparently great differences existing between these various statistics, for instance, between Gruby's report of 66 Mégnin's of 10 per cent, are due to slight errors which have not sufficiently been taken into account. I pointed out one of these when indicating the preferable technique which will make such an investigation fairly successful.

However, an important fact, admitted by all observers, and one which does not agree with Borrel's theory, is that young children never are the hosts of Demodex. Now, many cases of children attacked by leprosy have been noticed; according to Sauton the disease often manifests itself in them at the early age of 4 or 5 years.[8]

It may be interesting here to report some observations on the kinds of sebaceous glands inhabited by Demodex. In this connection, we must distinguish between normal sebaceous glands and obstructed ones which give birth to comedones (blackheads) and to the different varieties of acne. The parasite often lives in perfectly normal glands.

Comedones (blackheads) are formed in glands the openings of which have been obstructed, and as the glands continue to secrete, they sometimes swell by the accumulation of their own products. The plug is formed by a portion of sebum which has hardened in the same way that the majority of vegetable and animal oils thicken by contact with the air, that is, by oxidation. The formation of this plug is assisted by dust which adheres to the surface of the sebum. This explains the more frequent existence of comedones on persons who are careless in personal cleanliness. However, want of cleanliness is not the principal cause of comedones; they are influenced chiefly by personal predisposition, either because the sebum of certain individuals is naturally thicker, because dust sticks to it more readily, or because it contains substances which tend to harden more rapidly by oxidation. For instance, one meets people of the upper classes who are exceedingly careful in their personal habits, but who suffer great annoyance, from comedones and on whom they persistently reappear in spite of every care. On the contrary, there are workmen and beggars who certainly do not wash every day who have no comedones. I may also add, that persons subject to fatty seborrhœa, not too intense, provided they wash the face with care, often have no comedones in spite of the abundance of sebum; this is probably because the latter is soft and rapidly evacuated.

I mention these well-known and apparently insignificant details to show that Demodex may wrongly have been designated as the cause of comedones. Besides, and this brings us back to our subject, in studying the content of some hundreds of sebaceous glands, I found Demodex much oftener in normal ones, with open orifices, than in comedones. Balzer had already noted the same thing. This might have been expected

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[8] Sauton. La Léprose (1901), 327.

a priori. The invasion of a sebaceous gland by the larva or eggs of Demodex being possible only by the orifice of the excretory duct, those glands which are obstructed by comedones are protected from infection. Any parasite found in them can only have penetrated there before the formation of the plug.

If parasites which have previously penetrated glands bearing comedones should generate larvæ, the larvæ can not spread until after the expulsion of the comedone. Now, the latter are known to persist sometimes for months; indeed, I have met with some that I could extract only with the bistoury. Old comedones are often definitely encysted and the gland ceases to perform its function. In short, comedones are not habitually due to Demodex and they are unfavorable to the propagation of this parasite.

However, I did encounter Demodex on a leper who had severe acne molluscum which had infected a great part of his face, but the sebaceous glands taking part in this acne performed their functions abundantly and on the slightest pressure their product escaped easily.

I have been able more precisely to fix the percentage of lepers having Demodex than I have that of persons in health harboring this organism. My observations have been made on a hundred lepers. I collected the product of the sebaceous glands from all parts of the body, but more especially from the sides of the nose and the ear.. To judge from this series, the average percentage of lepers harboring Demodex does not seem to exceed 25.

I must say that in this search for Demodex on lepers Borrel has been more fortunate than I. He says, "Among the lepers we examined, we each time found Demodex in the follicles."[9] However, he does not mention the number of patients he examined. His investigation was made on the lepers in the Hospital Saint-Louis in Paris,[10] in so far at least as regards the direct search for Demodex in the follicles. The examination of microtomic sections of tumors was made from leprous nodules of the nose which he received from Algiers and Bergen. Borrel speaks only of one of these nodules, of which he gives an excellent description, but he does not say whether he found Demodex in the others, nor how many tumors he received. Therefore it would be difficult to form a statistical argument from his report "Sur les Acariens et la Lèpre." His discussion on the function of Acarina in Cancer is richer in material and, if one may reason by analogy between two such different diseases as leprosy and cancer, this comparison would afford some grounds for his hypothesis.

If the results of my researches on the lepers of San Lazaro are accepted, they will constitute a second unfavorable conclusion to Borrel's hypothesis, the first being that drawn from the absence of Demodex among young children.

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[9] Acariens et Lèpre. *Ann. Inst. Past.* (1909), 23, 127.

[10] When I had the opportunity of examining the lepers at the Hospital Saint-Louis a few years ago, they were about fifteen in number. I do not know how many there are at the present time, nor whether M. Borrel looked for Demodex in all of them.

It seems, in fact, that if Demodex were either the principal or the only agent for the propagation of leprosy, this parasite would be found in all, or, at least, in the greater number of lepers. However, this objection thus formulated would be too absolute, as the reply might be made that the infecting parasite would necessarily exist in the skin of the leper at the time of infection, but might well disappear later during the evolution of the disease. *Demodex folliculorum* is not a migratory parasite, it never changes its home: the same follicle is its cradle and its grave. However, it might be that the leprous lesions, with their dreadful ulcerations, render the follicle uninhabitable, or possibly bring about the death of the parasite. This must be the case once the ulceration has appeared. I have never found Demodex in an ulcer however recently it has been opened.

For this reason I pursued my investigations principally on the sebaceous glands from parts of the body which either were healthy, or on those (especially the nose and ears) which were only beginning to show symptoms of leprosy, and also on the sound skin which covered the beginning leprous nodules. From this long series of examinations, which includes several hundreds of sebaceous glands, I obtained the following results.

As already stated, *Demodex folliculorum* was not of frequent occurrence, it being found only on about a quarter of the lepers. It was not more frequent in the follicles of the leprous parts on the face than in the corresponding healthy parts. It was never encountered anywhere in the body except in the glands of the face or ears, either upon direct examination of the contents of the sebaceous glands or of microtomic sections of young nodules excised either from the living or the dead; and, moreover, it was never found in the normal skin of the hands and feet, either of healthy persons or of lepers.

The leprous spots that are met with in anæsthetic leprosy in all infected parts of the body including the face, for example, the livid or colored spots, and those invisible areas recognizable only by their anæsthesia, are free from Demodex. There are even places where the sebaceous glands are half atrophied, shriveled, small, and performing their functions improperly.

On the other hand, I have sometimes encountered *Demodex folliculorum* in the glands of the nose, ears, and chin, when these parts were already manifestly leprous. In such cases they were often found together with the bacillus of Hansen. I also have seen *Demodex folliculorum*, together with the Hansen bacillus, in the enormous follicles of acne molluscum in the case mentioned above. This is noteworthy, because it shows that Demodex and the bacillus can live together, and consequently, that if the former is not always found in the nonulcerated leprous parts, it is not because the bacillus has made such parts uninhabitable for it, but simply because Demodex has not always been established there. Lastly, I have found this parasite also in healthy follicles on lepers, where microscopic examination did not show the bacillus of Hansen to be present.

In brief, *Demodex folliculorum* appears only in a quarter of the lepers. When present, it is encountered in those parts of the skin already attacked by leprosy, provided the leprous lesions have not as yet seriously disorganized the tissues. It can also be found in the parts and in the follicles free from leprous infection. It is often absent from those parts affected by leprosy, even when this infection is recent. It is to be noted particularly that *Demodex folliculorum* is never encountered in the skin of the hands and feet, the parts particularly prone to the lesions of leprosy.

It is evidently difficult to make the above observations harmonize with the hypothesis that *Demodex folliculorum* is the principal agent transferring infection in leprosy; but the study of the lesions of leprosy suggests another and more important doubt, which must at once have impressed the reader of Borrel's report. The latter was led, as he admits,[11] after his researches on the same subject in cancer, to suspect the infecting action of an acarid in leprosy. However, is there any analogy?

The cancers discussed in Borrel's paper are epitheliomatous; with the exception, perhaps, of cases of metastasis, they are primary lesions in the places where they are found. One can understand that an external parasite can have deposited, at the place itself, the yet unknown virus of cancer. Can the same be said of leprous lesions? Would a leprologist think that the phenomenon of the anæsthetic spots, for instance, has its origin in the skin? Certainly not: it is a nervous manifestation. The same must be said of the mutilations and deformations of the extremities which so terribly afflict the unfortunate lepers. They are trophoneurotic troubles in the mutilating lesions, paralyzing in the deforming ones. Even were it not physiologically evident, the many works which have appeared on the pathologic anatomy of the nervous system of lepers have amply demonstrated this fact. A striking and common symptom in the leprosy is the moniliform transformation of certain nerves of the limbs, for instance, the ulnar and sciatic; these are often found by palpation in the hyperesthetic period before the mutilations and the deformations have appeared.

If we now pass from these important lesions to the ulcers and from the latter to the nodules which preceded them, and then to the simple turgescences which preceded the nodules, the question arises: Is the cause of these phenomena to be sought for in the skin, or in the glandular apparatus? The microtomic sections of the nodules show them to be full of bacilli, their formation to be due to the accumulation of these bacilli, and, doubtless, also to their toxic products.

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[11] *Ibid.* 125.

Contrary to Una's theory, it is now known that the bacilli of leprosy, at least for the most part, are contained in the cells. Some authors even say that they are found only in the cells; this last opinion seems to me open to dispute, but it is unnecessary to discuss the question here; it is sufficient to state that the greater number of bacilli are intracellular and that in these cells they undergo a process of destruction; a very large number are separated into granules. Their aspect recalls *in vivo* Pfeiffer's phenomenon *in vitro:* agglutination and destruction. One can follow all the series of the stages of this disorganization, from the simple vacuolated form to the reduction into smaller dissociated granules. In short, there is an evident phagocytosis. This phenomenon appears more clearly in the sections treated with crystal-violet-Gram.

The first thought suggested by this examination is that the nodules are produced by a defensive reaction of the organism, just as are the pulmonary tubercles of phthisical patients; they are a means of first collecting, then destroying, and finally of eliminating the bacilli. Such is the opinion of many leprologists; and even if we admit, with others, that the cells of the nodules contain bacilli in process of multiplication, this must be looked upon merely as a case of accidental insufficiency in the action of the former. But if this be so, the skin of the leper should much more be considered as a means of elimination than as an open door for infection. It is true that Babès thinks that both these functions may be attributed to it, as we shall show below.

Although it is a slight digression, I wish here to compare the sections from cutaneous nodules with those taken from the tissue of the spleen. It seems that the spleen also has a defensive function in leprous infection, as in several other diseases. It is certainly a collector of bacilli: the circulation brings them to this organ as to a storehouse. A very large number of these organisms are still perfectly normal, scarcely vacuolated;[12] next to them one finds others, more or less dotted, and a great quantity of others in fragments up to the final stage of reduction.

Other organs of the body also work with the same defensive aim; one sees such a process in the nodules of the moniliform nerves. At one autopsy I likewise collected numerous calcified concretions on the peritoneum, which contained the bacillus of Hansen undergoing destruction.

It appears that the spleen can exercise a defensive function better than the skin or nerves, perhaps because of a more energetic activity which it possesses in the work of destroying the bacilli, and in consequence also of the abundant circulation of which it is the seat. The spleen also seems better protected from the serious hypertrophies which manifest themselves in the cutaneous tissues and in the nerves. The nodules of the moniliform nerves are due to the accumulation of the bacilli and to their toxic products, but in this situation the bacilli can remain, as there is no powerful circulatory current compelling them to move. The same conditions surround the cutaneous nodules and the latter, after having defended the organism by localizing and digesting the bacilli, end by becoming victims of their own work; the cells deteriorate and succumb for want of power to rid themselves rapidly enough of the parasites and their products. Such deteriorated cells can be seen in all sections of the cutaneous nodules. The nodule in the end becomes disorganized and degenerates into an ulcer.

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[12] All normal bacilli seem more or less vacuolated when the staining of the sections has not been sufficiently prolonged, or when the decoloration according to the method of Ziehl or Gram has been carried too far. On the contrary, with good staining, one always finds many individuals uniformly colored.

The conclusions to be drawn from these theoretical views and the observed facts may be summed up as follows:

1. The external lesions of leprosy, not only the deformations, the mutilations and the anæsthetic areas, but even those disturbances which end in the formation of the cutaneous nodules, do not primarily originate at the point where they are observed, but are dependent on deeper causes, some simply nervous, others circulatory.

2. The accumulation of leprosy bacilli in the hypertrophies of the skin is the result of *an exportation from the interior of the organism*, the object of these formations being to localize, to destroy, and to eliminate the bacilli.

It seems as if this reasoning is but an argument against the theory of the transmission of leprosy by means of the skin. I do not wish to overrate its value, for I myself retain doubt on the question.

Although these ideas are fairly generally accepted by authorities on leprology, it must be acknowledged that they contain as much theory as observation. Now, a theory is most useful in guiding the seeker, but nothing is more dangerous than to regard it as an accepted truth, instead of a means of arriving at the truth. Moreover, I do not wish to present my observations as conclusive, for, if I believe others to be mistaken, I see no reason why they should not think the same of me.

If the cutaneous lesions of leprosy are reactions due to internal, nervous and circulatory causes, it does not follow that the contagion may not first of all have entered through the orifices of the skin, for it may be true that the first bacilli enter by means of the skin in the neighborhood of the parts where the nodules afterwards have formed. One can imagine these organisms gaining admission through the sebaceous glands, then penetrating deeper into the tissues and multiplying there, and lastly, a part of them stopped in their migration, and brought by the circulation into the parts near which they had entered. This would more or less explain the only fact which seems to favor the theory of infection through the sebaceous glands: namely, the parts where the first manifestations of leprosy are found are the sides of the nose and ears. However, it must be acknowledged that this hypothesis is purely without foundation. I suggest it, because in doubtful questions no possible hypothesis should be neglected. Cornil and Babès in 1888 thought that the integument, the sebaceous glands, and the follicles of the hairs in particular are a means, not only of elimination, but probably of the penetration of the bacilli also.

Whether this theory is true or not, I think I may conclude from all that precedes, that (1) it is difficult to reconcile the observed facts with the hypothesis that *Demodex folliculorum* is the principal agent of leprous contagion; and (2), that no positive argument can be drawn from the existence of external leprous lesions to prove that contagion takes place by way of the skin.

II.

So far we have considered Borrel's theory of the contagion of leprosy by acarids more particularly with regard to the place where the bacilli might be introduced and where they might multiply. It remains for us to consider the agent itself, which Borrel supposes to be the bearer of the contagion, and to ask if it possesses the qualifications necessary for this function.

The genus Demodex, the only one of the family *Demodecidæ*, comprises only one species, *Demodex folliculorum* Simon, which is divided into several vareties, of which only one appears to live in the human skin, the var. *hominis* Simon.

Besides Demodex, the acarian parasites of the human skin thus far encountered are the following: *Sarcoptes scabiei* Latr., parasite of the itch, Sarcoptes of the Norwegian itch, the identification of which is uncertain and which perhaps is only a variety of *Trombidium holosericum* Herm.; various species of Ixodes and Argas. There are probably some other acarian parasites of man as yet but little understood. Demodex is the only fixed acarian parasite known to live in the human skin; the others cited are all more or less migratory.

Borrel states as follows: "Lepers must be infected by Demodex or other fixed acarids. I found it impossible to determine on the sections, the species or variety of the parasites I saw."[13] Why should the suspected parasite be fixed? Is not a migratory acarid more to be feared? It is precisely this sedentary character of *Demodex folliculorum* which seems to me to afford the best argument against Borrel's theory. We have seen that one often meets with areas of the skin quite recently attacked by leprosy, the follicles of which contain no Demodex; this fact would easily be explained if the acarid, bearer of the contagion, were migratory; it can not be explained if it is fixed. Besides, how should Demodex carry the contagion from one person to another?

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[13] *Ann. Inst. Past.* (1909), 23, 127.

Borrel states that the conditions of migration of Demodex are unknown.[14] It is true we have not as yet a complete account of its life history, but the few facts which seem well established are sufficient to show that *Demodex folliculorum* stays at home. No observer has met with it outside the sebaceous glands. For my part, I have often examined the scrapings of the skin near the glands containing Demodex; and I did so periodically in the particular case of an individual infected with the parasite, but with negative results.

Moreover, the anatomy of Demodex renders it unfit for the work; its legs, consisting of only three very short articulations instead of five as with the migratory acarids, such as *Sarcoptes scabiei*, are exceedingly small; they resemble little conical tubercles and it seems hardly possible that they could carry the animal's enormous abdomen. In fact, when Demodex is observed under the microscope, it is very easy to see the difficulty it experiences in moving even a few tenths of a millimeter, and this difficulty is increased by the mass of sebum in which it is embedded. Therefore, the individuals of Demodex are prisoners, so to say, in the sebaceous gland in which they have been developed, living normally in the lowest parts, with the head generally turned to the bottom. Their reproduction takes place in their prison. Nathan Banks thinks that, if the Demodex lays eggs, they must be fusiform,[15] but I think he is mistaken. I have never met with true eggs of the parasite; one must probably admit with Mégnin[16] that what have been taken for eggs really are apode larvæ. As these develop, they acquire six little unarticulated papillæ which represent the legs, and then, by successive moults, the eight pairs of articulated legs of the adult.

These larvæ are carried out of the gland with the mass of sebum as it escapes, little by little, and they alone could transport the contagion of leprosy, but only in the same way as the sebum itself, and the residue of the cells and other particles that it contains could do the same thing. Evidently the sebum, the particles, and the Demodex larvæ may be covered with the Hansen bacilli and may disseminate them; but this would result only in a passive contagion. The idea then must be abandoned that Demodex is an active propagator of leprosy, as, for example, is, in some diseases, the mosquito or glossina which has sucked the virus of a patient and which then inoculates another individual by stinging him.

I have often looked for the Hansen bacillus in the body of Demodex, but without success; I can not say that it never penetrates the body, for to prove this would be difficult, but the preceding considerations render this question unimportant.

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[14] *Ibid.*

[15] A Treatise on the Acarina or Mites, *Proc. U. S. Nat. Mus.* (1905), 28, 1.

[16] *Loc. cit.*

I have had no opportunity to study the migratory acarids cited above from the point of view of leprous contagion, except *Sarcoptes scabiei.*

This acarid is essentially migratory. The female alone forces its way into subepidermic tunnels which she has burrowed for the purpose of laying her eggs, and remains in this situation until she dies; the male raises a small epidermic pellicle under which he hides, but this is only a temporary shelter and he soon leaves it to form a similar one elsewhere, and so on. The remainder of the life of these parasites is passed on the surface of the skin.[17] Here, no *a priori* objection can be raised against leprous contagion by the medium of the Sarcoptes of the itch. It is a mere question of fact.

I observed an epidemic of the itch among the lepers of San Lazaro and learned from questioning them that the greater number of the lepers then afflicted with the disease did not have it before entering the hospital as leprous patients; moreover, I saw the itch in an early stage on several of the lepers. Finally, several of the lepers told me that they had never had the itch previously. If their assertions can be trusted, I must at least conclude that the Sarcoptes of the itch is not the normal agent of leprous contagion.

I have sometimes encountered the Hansen bacillus in the parts affected by the itch, particularly when a leper, by scratching, has caused erosions which suppurated; but as the erosions were in the immediate vicinity of leprous ulcers, it is not proved that the bacilli had been imported by the Sarcoptes. I have never found the Hansen bacillus in the itch furrows formed in parts not previously leprous. On triturating bodies of Sarcoptes for bacteriologic examination, I did not find the bacillus of leprosy.

Finally, I treated and cured several cases of itch on lepers, and after the disappearance of all signs of the infection, the healed parts after an observation carried on for several months showed no symptoms of leprosy. However, evidently no great importance can be attached to this last statement, as we are entirely ignorant of the duration of the incubation period of leprosy.

From all this, only a negative conclusion can be reached, since we have no conclusive proof that the Sarcoptes of the itch is the normal agent of leprous contagion; but neither is there proof that it can not transmit leprosy accidentally.

There remain two other acarids which I have encountered among lepers, but which, for want of sufficiently detailed literature, I can not determine definitely. One is of a species of the genus Tyroglyphus, the other of a species similar to this genus.

[17] Mégnin, *loc. cit.* 219.

I sometimes met with the first species in leprous ulcers. I found it also in many cases of suppurative dermatitis following an infection of the itch and in the erosions caused by scratching. Some of the cases were very severe, and one might even have thought the lesions to be leprous manifestations; the feet and the lower part of the legs in particular were tumefied, very painful, the derma was exposed in many places and yielded a continuous flow of seropurulent fluid. The fact that two or three of these patients had leprous ulcers coexisting on the feet made it all the easier to mistake this infection for an exacerbation of acute leprosy. However, this disorder was due solely to the acarid of which I speak; in fact, the bacteriologic examination of the pus, of the serum, or of the scrapings of the diseased parts revealed no Hansen bacilli except at the precise place of the preëxisting leprous ulcers; the disease yielded in a few days to the specific treatment for itch, and nothing was afterwards seen on the skin except the well-defined leprous ulcers which were there previously.

This is not the first time that the presence of Tyroglyphus or some other saprophytic acarid has been remarked in ulcers, or in neglected sores, as is evidenced by all doctors who have treated sores of long-standing, ulcers, cancers, etc., among the poor and persons not scrupulously clean. Leprologists themselves have often noticed it. I call attention to it because of one point which touches on our subject; that is, that neither in analyzing the pus nor in examining acarians themselves, was I able to discover the Hansen bacillus except at the exact place of preëxisting leprous ulcers, or in their immediate vicinity. This fact is all the more significant because Tyroglyphi are very migratory acarians and even fairly active ones, and also because the suppurative dermatitis is confluent with leprous ulcers.

From this statement it seems that Tyroglyphi also should be eliminated from the number of normal bearers of the contagion of leprosy.

I wish merely to mention the other acarid of which I spoke and which appears to be similar to the genus Tyroglyphus. It presented an unexpected characteristic, for I discovered it not in open ulcers but in the serum from small, closed phlyctenæ. I was unable, in any of my observations with the magnifying glass, to find the opening by which this parasite made its way through the epidermis. As it was found on two patients infected with the itch, and as these phlyctenæ were near the furrows of the itch on one patient especially, it is a question whether there is any connection between its work and that of the Sarcoptes or just what this connection may be. Certainly there is no relationship, for these two parasites differ as much from each other as does Sarcoptes of the itch from Tyroglyphus. On the other hand, this new acarid, judging from its habitat, is not a saprophyte, but a parasite. No acarian parasite within the human skin is known at the present time except Sarcoptes of the itch and Demodex.

ON THE OCCURRENCE OF AN ACCESSORY NASOFRONTAL DUCT OF THE FRONTAL SINUS.[1]

By Elbert Clark.[2]

The great variability in the size and extent of the frontal sinus, its position within the frontal bone and its relation to the ethmoidal cells have been well shown by Killian,(2) Onodi,(6) and Zuckerkandl.(12) This structure is indeed so variable that one is inclined to ask if there is any one type of frontal sinus which may be considered normal or distinctly typical. Therefore, it is not surprising that a difference in nomenclature as well as often some confusion have arisen. It has recently been shown by Wilson(10) that the nasofrontal duct and the ostium frontale are subject also to almost as great variations as the frontal sinus; and further, that in approximately only 55 per cent of the cases that cavity in the frontal bone, usually termed the frontal sinus, is drained by the duct which is the upward continuation of the infundibulum ethmoidale. In the other 45 per cent it opens into the middle meatus.

In the anterior ethmoidal region in the immediate vicinity of the sinus frontalis the number of ethmoidal cells (including the sinus frontalis) may vary from one to four (rarely five); these are variously known as bullæ frontales, anterior ethmoidal cells, etc. They are termed frontal cells by Killian.(2) They usually open into a common vestibule, more or less well developed, and are often fused and communicating in their upper portions. In the fœtus and infant they are seen as membranous evaginations from a slight ethmoidal bulla at the upper extremity of the infundibulum ethmoidale. These Killian(5) designates as the first, second, third, and fourth frontal cells. Either one of these cells may be represented in the adult by the frontal sinus. The frontal sinus may develop from the *Anlage* of either, the relations in the adult varying accordingly. This cell is usually the largest of the four and in a majority of these cases is a direct continuation of the infundibulum. That frontal cell which is located within the frontal bone is termed by Killian(2) the sinus frontalis, although it may not open into the infundibulum ethmoidale. The frontal sinus in this instance is not to be considered as one of the frontal cells. In many skulls four of these anterior ethmoidal cells are seen.

The present dissection was made on a specimen from a negro subject which was preserved in Kaiserling's fluid, allowed to dry for two weeks and softened by standing overnight in water. The drying seems to make the specimen more suitable for the separation of the membranous from the bony structures. It is possible by this method to chip away as much of the bone as is desired, leaving the membranes of the nasal and accessory nasal cavities undisturbed in one continuous piece, the relations of which are then easily determined. A successful preparation is obtained more easily in this manner than after mere preservation in formalin without the drying. In a subject that had been preserved in 50 per cent formalin and dried for two years, the membranes lining the frontal, maxillary and sphenoidal sinuses, the ethmoidal cells and nasal passages were entirely freed from bone, and a membranous model of all these cavities was obtained in one unbroken piece which was mounted on a portion of the occipital bone left undissected. In the negro subject the supraorbital ridges were prominent and the skull, nasal and cheek bones thick. The frontal sinuses of both sides were fairly large, of about equal size and approached the median line where they were separated by a thin lamina of bone.

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[1] Published from the Anatomical Laboratory, Philippine Medical School, Manila, P. I.

[2] From the Hull Laboratory of Anatomy, University of Chicago.

The frontal sinus of the left side (see Pl. I, fig. 1) is 30 millimeters in its mesial-lateral diameter, 28 millimeters in the saggital, and 12 millimeters in the antero-posterior diameter. Its lower surface is on a level with the cribiform plate and is 8 millimeters above the fronto-ethmoidal suture. On either side a middle and a posterior ethmoidal cell,[3] which opens into the superior meatus, covers over the entire roof of the orbit behind the frontal sinus. The other ethmoidal cells are small, as are both maxillary sinuses. The sphenoidal sinuses are not excessive in size. The left frontal sinus opens through the nasofrontal duct into the infundibulum ethmoidale. Its relations are those usually given for this sinus. The frontal sinus on the right side is in relation to three other frontal cells, the sinus itself representing the second cell. The first frontal cell is situated mesial and below and in close relation to the accessory duct of the sinus. (See Pl. I, fig. 1.) The third and fourth are small, narrow cells, 1 and 2 millimeters in diameter, respectively, and lie in close opposition to the posterior surface of the sinus frontalis, between it and the ethmoidal cells which cover over a greater part of the orbit. (See Pl. I, fig. 2.) The first, third and fourth frontal cells open into a small vestibule which is a direct continuation of the infundibulum ethmoidale. The frontal sinus (second frontal cell) on its posterior inferior funnel-like surface also communicates with the vestibule through a very short rudimentary nasofrontal duct. It presents a striking peculiarity in the occurrence and course of an accessory ductus nasofrontalis. Connection with the infundibulum and the middle meatus is attained only through the common vestibule of frontal cells 1, 2, 3, and

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[3] Ethmoidal cells of highest meatus of Killian's cellulae ethmoidates A and B, Plate I, fig. 2.

4, by the rudimentary nasofrontal duct just mentioned. The accessory naso-frontal duct arises from about the middle of the inferior surface of the sinus, 12 millimeters lateral from the median line. It takes a perpendicular course downward for 12 millimeters where, in a bulbous enlargement of 5 millimeters, it comes in close opposition with the saccus lacrimalis and the upper extremity of the ductus nasolacrimalis, and after curving through an angle of 90° extends medianward for 8 millimeters on the sutura frontolacrimalis just posterior to and above the ligamentum palpebrale mediale. Here it leaves the sutura nasofrontalis and runs downward, medianward and anteriorly in the os frontale and then beneath the os nasale to open into the anterior portion of the fossa nasale, 12 millimeters below the sutura nasofrontalis. The duct in its first course downward and medianward, after leaving the frontal sinus, curves around the first frontal cell above referred to and lies in close opposition to it, a very thin lamina of bone separating them.

The arrangement of the four frontal cells, of which the frontal sinus represents the second, will conform to the method of development of the frontal sinus from the infundibulum advocated by Killian, which is as follows: In the human fœtus five small ridges and six small furrows are to be seen on the lateral wall of the nasal cavity. In front of these is the small nasoturbinal elevation, and below all of these structures a long, narrow, horizontal ridge, the maxillo-turbinal. The maxillo-turbinal gives rise to the inferior concha, the nasoturbinal to the aggar nasi and the processus uncinatus and the five small ridges to the middle and superior conchæ and to a fourth concha when present. The bulla ethmoidale develops posterior to the processus uncinatus and the adjoining first furrow and below the first ridge (the *Anlage* of the middle concha). The anterior furrow, on becoming deeper, thus forms the hiatus semilunaris and the infundibulum ethmoidale. By outward budding of the membrane there arise upon the anterior and superior aspects of the infundibulum the four primitive frontal cells. These are separated by narrow, incomplete septa, the infundibulum thus becoming a cavity with four branching evaginations. Further development is slow until about the age of puberty. The evagination which extends into the os frontale is termed the sinus frontalis. It may be either one of the four. The relations of the frontal cells in the adult vary accordingly. Killian terms this the indirect mode of development. When the infundibulum does not acquire the four evaginating appendages, but forms only one direct evagination anteriorly into the os frontale, there follows the direct mode of frontal sinus formation. In this latter case no frontal cells are present other than the sinus frontalis.

According to Mouret, that membranous evagination which develops first in the anterior ethmoidal region from the superior lateral wall of the nasal cavity forms the frontal sinus. The relation to the other ethmoidal cells and the variability of the nasofrontal duct are thus dependent upon whichever anterior ethmoidal evagination develops first. This would also explain how a great proportion of the frontal sinuses are not in connection through the nasofrontal duct with the infundibulum ethmoidale. Ernst Witt claims that the sinus frontalis and the cellulæ ethmoidales arise from *Anlage* which developmentally are related very closely and which may replace one another.

It is difficult to account embryologically for an accessory nasofrontal duct in this position. A possible explanation might be afforded if we assume that coincident with the development of the evaginations from the infundibulum, there developed from the upper anterior wall of the fossa nasalis a long, slender evagination—a bulla nasalis anterioris—which came to lie in the position described for the ductus nasofrontalis accessorius, and which later established a communication with the sinus frontalis by fusion; or, on the other hand, if we assume, instead of a bulla nasalis anterioris, that from the sinus frontalis itself, the long evagination developed and later established communication with the fossa nasalis. In addition, it is possible that the sinus frontalis represents the dilated upper extremity of the bulla nasalis anterioris, and that communication with the vestibule of the frontal cells was attained by fusion as above.

In conclusion I desire to thank Prof. J. Gordon Wilson for the kind assistance he has given me in the identification of the structures described.

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ILLUSTRATION.

PLATE I.

FIG. 1. Illustrating the course of the ductus nasofrontalis accessorius. The frontal sinus, nasal cavity and neighboring structures of the right side are seen from in front. The anterior part of the nose, the os nasale, most of the os frontale and the anterior part of the maxilla have been removed. The size and relations of the sinus frontalis and the first frontal cell are well shown. The ductus nasofrontalis accessorius is seen to spring from the inferior surface of the sinus frontalis, to run downward into close proximity with the saccus lacrimalis in a dilatation, then to proceed medianward (on the sutura frontolacrimalis) and on downward (beneath the os nasale) terminating at its ostium in the anterior part of the fossa nasalis.

2. The cellulæ ethmoidales, ductus nasofrontalis accessorius and lateral wall of the nose of the right side seen from above and from the mesial side. The relations of the first, second (sinus frontalis), third and fourth frontal cells are to be seen. The upper portion of the third frontal cell has been cut off to show its opening into the common vestibule. The rudimentary ductus nasofrontalis can not be seen. The sinus frontalis is slightly distorted to show the structures beneath its mesian portion.

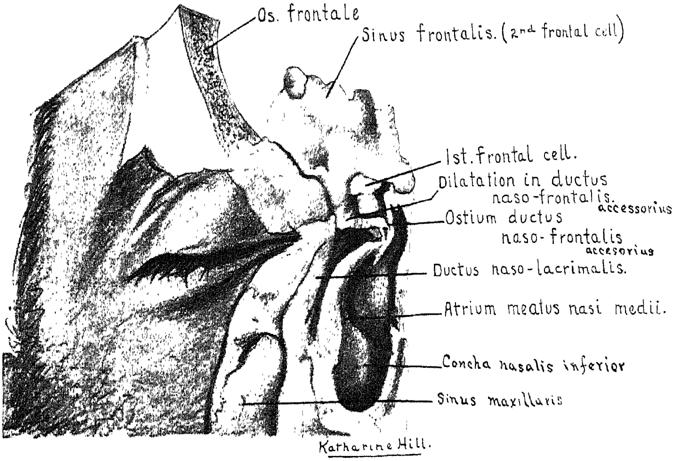
Os. frontale
Sinus frontalis. (2nd frontal cell)
Ist. frontal cell.
Dilatation in ductus naso-frontalis. accessorius
Ostium ductus naso-frontalis accesorius
Ductus naso-lacrimalis.
Atrium meatus nasi medii.
Concha nasalis inferior
Sinus maxillaris
Katharine Hill.

FIG. 1.

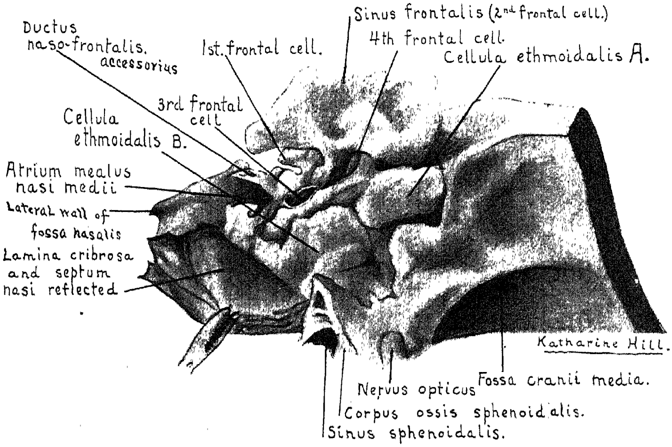

FIG. 2.

PLATE I.

A NOTE ON THE SPONTANEOUS OCCURRENCE OF BACILLARY DYSENTERY IN MONKEYS.

By Fred B. Bowman.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

The epidemiologic factors in the etiology of bacillary dysentery are somewhat obscure. The sudden appearance of acute cases in districts usually free of the disease has been attributed to various causes. Drinking water and human carriers are known to be sources of infection and animals have been suggested as possible factors. The following report indicates that the latter may in reality be a source of infection for human beings.

During March and April, 1910, several cases of severe dysentery developed in monkeys kept in the animal house of the Bureau of Science. Two animals which had been used several months previously in an experimental investigation on trypanosomiasis were found in a condition of extreme prostration similar to that seen in acute human bacillary dysentery and were turned over to me for further study.

The animals were chloroformed and autopsies were performed. The following excerpts are taken from the protocols.

> Only the rectum and colon are affected, the small bowel shows no abnormal condition. The mucosa of the intestine is markedly injected, showing patches of hæmorrhage, and is covered with a sticky coating of bloody mucus. Microscopic examination of the fæces shows a large amount of mucus, some blood, leucocytes, and degenerated epithelium. Ova of *Œsophogostomum* are present and cysts caused by this parasite are seen in the intestinal wall.

Some of the mucus portion of the stool was suspended in salt solution and after a short time plates were made from the surface of this suspension, lactose-litmus-agar being used. In twenty-four hours no red colonies were present, the predominating type being extremely small, clear and blue. Cultures from the heart's blood, liver and spleen were negative. Control plates from the stool of a monkey apparently well showed large numbers of red colonies.

Cultures were made on agar slants from these small, blue colonies and later the following agglutination tests were performed, parallel ones being made at the same time with a typical nonacid-producing dysentery organism of the Shiga and an acid-producing one of the Flexner type. Antidysenteric sera from rabbits which had been immunized by Dr. E. R. Whitmore of this laboratory were used, one agglutinating specifically the acid type of organism and the other that of the nonacid type. Table I shows the dilutions employed and that the organisms from monkeys numbered I and II were both agglutinated by the nonacid strain, and in the same dilutions as the true acid strain used in the same experiment. They were not agglutinated by the Shiga serum.

Each organism was also tested as to its acid-producing and sugar-fermenting properties. (See Table II.) No acid was produced in lactose-litmus-agar, while the other four sugars used showed marked acid production. No gas was formed in any of the media.

No evidence is at hand which would indicate that these monkeys became infected from our laboratory cultures of the dysentery bacillus. A few rabbits were in the same animal house in the other end of the building. These animals had been inoculated subcutaneously with dysentery organisms five months previously, but they had never been placed near the cages containing these monkeys. The monkeys had been in the laboratory for months and it seemed highly probable that they had acquired the infection here.

If monkeys can be infected with bacillary dysentery, naturally it is not improbable that other animals may become carriers and give rise to the sudden appearance of this disease in previously noninfected districts. Only one observer has reported the production of the disease in monkeys by feeding experiments, and a search through the literature at hand fails to show a previous report of natural or spontaneous infection of monkeys with bacillary dysentery.

TABLE I.

Dilution	1–50.			100.			300.			500.			700.			900.			1,100.			2,200.		
Time (hours)	2.	5.	24.	2.	5.	24.	2.	5.	24.	2.	5.	24.	2.	5.	24.	2.	5.	24.	2.	5.	24.	2.	5.	24.
No. I organism:																								
Flexner serum	+ +	+ +	+ + +	+ +	+ +	+ + +	+	+ +	+ + +	—	+ +	+ + +	—	+ +	+ + +	—	+	+	—	—	+	—	—	—
Shiga serum	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Normal rabbit serum	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
No. II organism:																								
Flexner serum	+ +	+ +	+ + +	+ +	+ +	+ + +	+	+ +	+ + +	—	+ +	+ + +	—	+	+ +	—	—	—	—	—	—	—	—	—
Shiga serum	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Normal rabbit serum	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Shiga:																								
Flexner serum	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Shiga serum	+ +	+ +	+ + +	+ +	+ +	+ + +	+	+ +	+ + +	—	+	+ +	—	—	+	—	—	—	—	—	—	—	—	—
Normal rabbit serum	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Flexner:																								
Flexner serum	+ +	+ +	+ + +	+	+ +	+ + +	+	+ +	+ + +	—	—	+ +	—	—	+	—	—	—	—	—	—	—	—	—
Shiga serum	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Normal rabbit serum	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

TABLE II.

Media	Glucose litmus agar.		Lactose litmus agar.		Maltose litmus agar.		Saccharose litmus agar.		Mannite litmus agar.	
Strains.	Gas.	Acid.	Gas.	Acid.	Gas.	Acid.	Gas.	Acid.	Gas.	Acid
Shiga type	—	+ + +	—	—	—	+		+		
Flexner type	—	+ + +	—	—	—	+ +		+	—	+ +
Monkey No. I	—	+ + +	—	—	—	+ +	—	+	—	+ +
Monkey No. II	—	+ + +	—	—	—	+		+	—	+

COMPLEMENT FIXATION IN YAWS.

By Fred B. Bowman.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

There is still some doubt concerning the nosologic position of yaws; some eminent authorities believing it to be a modified form of syphilis, while others consider it a separate and distinct disease.

Castellani[1] in 1905 attempted to transmit the disease to a purple-faced monkey, but without success. However, in 1906, he was able to infect one out of three monkeys inoculated. This animal later was successfully inoculated with syphilis. Neiser, Bauerman and Halberstädter,[2] in 1906, found that all classes of monkeys could be inoculated with yaws and that monkeys immunized against syphilis did not become immune to yaws.

Castellani also applied the Bordet-Gengoũ reaction to yaws, following the technique used by Wassermann, Neiser and Brück,[3] and was able to demonstrate specific yaws antibodies and antigen. The following is a brief summary of his results:

"I. Extract of nonulcerated yaws papules containing *Spirochæta pertenuis* + serum from a monkey infected with yaws + complement (fresh guinea pig's serum) and later, sensitized goat corpuscles. *Result:* No hæmolysis.

"II. Same as I, but in the place of yaws papules extract, extract of leprosy nodules used. *Result:* Hæmolysis.

"III, IV and V. The same experiment was performed, using extracts or pseudogranuloma pyogenicum, syphilitic condylomata and syphilitic primary sore. *Result:* Hæmolysis.

"VI. Extract of yaws papules from six different cases of yaws and serum from a monkey immunized against syphilis. *Result:* Hæmolysis.

"VII. Extract of yaws papules and normal monkey serum. *Result:* Hæmolysis.

"VIII. Extract of Spleen juice from a case of yaws and serum of a monkey infected with yaws. *Result:* No hæmolysis.

"IX. Same as VIII, except that serum from a syphilitic monkey was used. *Result:* Hæmolysis."

Castellani sums up the preceding experiments by saying: "The above experiments show that it is possible to detect specific yaws antigen in the yaws papules and in the spleen of cases of yaws and specific yaws antibodies in the blood of monkeys treated with inoculation of yaws material."

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[1] *Journ. Hyg. Cambridge* (1907), 7, 558.

[2] *Münchener med. Wchnschr.* (1906), 53, 1337.

[3] *Deutsche med. Wchnschr.* (1906), 22, 745.

"Experiments IV, V, VI, and IX show also that yaws antibodies and antigen are different from syphilis antibodies and antigen and therefore syphilis and yaws differ specifically."

In 1906[4] Landsteiner, Neisser and Poetzl used an alcoholic extract of guinea pig's heart in complement-binding experiments with serum from cases of surra. This extract when employed with serum from patients with syphilis gives a positive reaction in 80 per cent of the cases, but it had never been used with serum from those infected with yaws. Therefore, I decided to subject the sera of yaws patients to the complement fixation test with this extract, in the hope of throwing further light upon the relationship of yaws to syphilis. The sera were taken from four children and one adult with well-marked cases of yaws having the typical incrusted ulcer, in smears from which numerous *Spirochæte pertenues* were found.

One gram of guinea pig's heart was ground finely and 50 cubic centimeters of 95 per cent alcohol added. The whole was then heated for three hours at 60 °C. and the clear fluid decanted. Red blood cells of the ox were used, and immune rabbit serum, which was hæmolytic when diluted 1 to 5,000, furnished the amboceptor.

Three preliminary experiments were always performed before the final Wassermann reaction, to determine the following:

1. Whether the extract was hæmolytic.

The extract was added to washed ox-blood cells in three dilutions, 0.4, 0.2 and 0.1, and allowed to stand one hour at room temperature.

2. Whether the extract inhibited hæmolysis.

The extract in dilutions 0.8, 0.4, 0.2, 0.1 and 0.05 + complement or fresh guinea pig's serum was allowed to stand one hour at room temperature (about 30° C.), then 1 cubic centimeter of a 5 per cent washed ox blood and 0.001 cubic centimeter amboceptor were added and incubated.

3. The serum to be examined 0.1 in each tube and salt solution 0.4, 0.2, 0.1 added in place of the extract and the whole allowed to stand one hour at room temperature. Then 1 cubic centimeter of washed ox blood and 0.001 cubic centimeter of amboceptor added.

It was found that the extract from the guinea pig's heart with the serum from cases of syphilis inhibited hæmolysis; that is, 0.1 cubic centimeter of inactivated serum from a case of syphilis + extract of guinea pig's heart (0.4, 0.2, and 0.1) + complement from fresh guinea pig's blood serum, and, in one hour, 0.001 amboceptor + 1 cubic centimeter ox-blood cells added, gave no hæmolysis. A parallel experiment performed at the same time, in which the same reagents were used, with the exception that yaws serum was substituted for the syphilitic serum, resulted in almost complete hæmolysis.

This experiment was performed many times, but always with the same result. These results demonstrated that serum from cases of yaws does not bind complement when the extract from guinea pig's heart is used.

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[4] *Wien. klin. Wchnschr.* (1907), 20, 1420.

An extract of yaws papules was then prepared. One gram of papule was added to 5 cubic centimeters of salt solution containing 0.5 per cent carbolic acid and placed in a shaking apparatus for twenty-four hours. This was then centrifugated and the opalescent fluid decanted and placed on ice until ready to be used.

This extract was tested in the same way as the guinea pig's heart and was found to be nonhæmolytic and also noninhibitive.

The extract in three dilutions, 0.4, 0.2 and 0.1, was added to the sera from the cases of yaws (0.05 cubic centimeter) — 0.05 cubic centimeter of complement. and allowed to remain one hour at room temperature; then 1 cubic centimeter of washed ox-blood cells + 0.001 cubic centimeter amboceptor were added and all incubated at 37° C. for two hours and then placed on ice for twenty-four hours before the final reading was made. At the end of twenty-four hours it was found that there was marked inhibition of hæmolysis.

The following table summarizes the results obtained with the two kinds of extract:

Extracts used	Yaws extract.			Guinea pig's heart extract.		
Dilution of extract	0.4	0.2	0.1	0.4	0.2	0.1
Yaws sera	—	—	+ +	—	+ +	+ + +
Syphilis sera	+ +	+ +	+ + +	—	—	+ + +
Normal sera	+ + +	+ + +	— — —	—	+ + +	+ + +

+ = hæmolysis.
— = no hæmolysis.

These experiments are confirmatory of and supplementary to those of Castellani already cited and furnish additional evidence of the non-identity of syphilis and yaws.

A GENERAL DISCUSSION OF PELLAGRA[1] WITH REPORT OF A PROBABLE CASE IN THE PHILIPPINE ISLANDS.[2]

By David G. Willets.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

Pellagra is a chronic or acute, afebrile or febrile, endemic and at times epidemic, probably noncontagious, systemic disease of unknown etiology, occurring chiefly among the poorer classes of maize-eating peoples. It is characterized clinically by a seasonal periodicity, a typical skin eruption, digestive disorders and nervous and mental disturbances, and pathologically by slight peculiar anatomical lesions.

The disease first occurred in Spain in 1735, and now is found extensively in Italy and Roumania, in Greece, France, Austria, northern Portugal, Poland, Turkey, Africa, upper and lower Egypt, the West Indies, various parts of South America, Barbados, Mexico, and in the United States, especially in the South Atlantic portion. Two cases have been reported from England, several from India, one from Porto Rico, and two from the Panama Canal Zone. Although the cultivation of Indian corn and its consumption as food occurs in parts of the world from which pellagra is not reported, yet pellagra is unknown in sections where maize is not used as an article of diet.

The original home of Indian corn and the date of its introduction into Europe are apparently debatable questions, but nearly all authors agree that pellagra was not known in Europe until maize growing and eating had existed for some time. King(6) claims North America as the original home of Indian corn and also of pellagra and states that Baruino, in 1600, described meagerly a condition among certain Indian tribes which doubtless was pellagra and that he thought it arose from eating maize.

Gaspar Casal, in 1762, reported pellagra under the name of *mal de la rosa*, having seen his first case near Ovieda, Spain, in 1735, and subsequently other cases in the Asturias (Asturiensis). It was found in other parts of Spain within a few years, and in 1893, 2 per cent of the Spanish peasantry were pellagrous. (Tuczeh).[3]

The disease appeared in Italy, in the Lombardy district, in 1750, and gradually spread to other provinces. It was clearly described by Frapoli, of Milan, in 1771, under the name of pellagra (from *pellis* –skin, and *agra*- rough), and, according to King,(6) Frapoli declared it to be an ancient disease known in 1578 as pellarella, as might be seen by reference to the regulations for admission to the Hospital Major of Milan at that time. The ravages of the disease have been most marked in Italy and Roumania, where it appeared in 1810. In Italy, in 1879 there were 97,835 cases; in 1881, 104,067 cases; in 1899, 72,603, and in 1902, 55,029 (Wollenberg).(26) In Roumania, in 1885 there were 10,626 cases: in 1886, 19,797; in 1898, 21,272;(6) and in 1906, 30,000 cases (Triller).[4]

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[1] Synonymy: Mal de la Rosa; Mal de Padrone; Lepra Scorbutica; Asturiensis; Mal de Sole; Vernal insolation; Mal de Miseria; Maladie de la Teste; Buba tranjilar; Maidimus; Psychoneurosis Maidica.

[2] Read at a meeting of the Manila Medical Society, October, 1910.

[3] Quoted by Lavinder.

The elder Hameau[5] reported pellagra from the vicinity of Teste, France, in 1818 (*Maladie de la Teste*) and Pruner[6] found it in Africa in 1847. It appeared in Corfu, in 1856, and Sandwith found it in Egypt in 1893. Ray[7] reported it in 1892, from one of the provinces of North Behar, India, and three physicians from India recognized photographs of cases of pellagra shown them by Sandwith in England as being typical of a condition they had seen in India, but had not understood. Two sporadic cases were reported in the United States in 1863 and 1864 by Doctor Gray, of Utica, New York, and Doctor Tyler, of Somerville, Massachusetts. Doctor Sherwell, of Chicago, found a case in a sailor on a ship in New York in 1902 and, in the same year, Dr. H. F. Harris,(4) of Atlanta, Georgia, reported a case of agchylostomiasis in a native of Georgia who had always resided in the State, presenting the typical symptoms of pellagra. In 1907, Searcy(17) described an epidemic of 88 cases in the Mount Vernon Hospital for the colored insane in Alabama. Since 1907 many articles relative to pellagra have appeared in American medical literature and many cases, especially from the insane institutions of the South Atlantic States, have been reported. The condition has become so serious in the United States that The National Association for the Study of Pellagra has been formed and the Surgeon-General of the Public Health and Marine-Hospital Service has appointed a commission to investigate the disease.

Since Marzari,[8] in 1810, associated pellagra with the eating of Indian corn, the majority of investigators of the disease have attributed it to the continued use of maize as a foodstuff; persons holding this opinion are known as the *zeists*, in contradistinction to the *antizeists* who consider the condition merely a symptom-complex occurring in alcoholics, insane persons, and in persons with other depressed symptoms (Lavinder).(7) However, the zeists differ widely in their beliefs as to just how the disease is caused by a diet of maize. Thayer(20) divides the opinions of this school into four classes, as follows: (1) Toxic substances are produced by changes occurring in healthy maize in the process of digestion (Neusser); (2) the poisons are chemical substances arising from the decomposition of maize before ingestion (Lombrosso); (3) the disease is caused by the products of changes produced [in maize] by various special micro-organisms and bacteria (Majocchi and Cuboni); (4) it arises from changes produced [in maize] by various molds (Ballardini, Gossio and Ferrati, Ceni, Fossati).

Lavinder summarizes as follows the reasons why the ideas of the zeist school can not lightly be passed over:

"(1) The disease is an endemic one confined largely at least, if not exclusively, to populations which grow and eat corn and more especially to those who, through force of circumstances, eat a poor grade of corn. (2) By far the great majority of thinkers and students believe the disease to be in some definite, if at present rather ill-defined, way connected with the use of corn as a foodstuff. (3) Italian and other authorities, in their attempts to limit and eradicate pellagra, base all prophylactic measures almost entirely upon this theory and, as an outcome of such means, good results are claimed."

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[4] Quoted by King.

[5] Quoted by Lavinder.

[6] Quoted by Sambon.

[7] Quoted by King.

[8] Quoted by Taylor.

Sambon,(13) in 1905, referred to the United States as a conspicuous example of a maize-growing, maize-eating country which did not have pellagra, but, prior to June, 1909, Williams,(11) of South Carolina, obtained records of about 1,000 cases in that country, most of which were from asylums. It is variously estimated that at present there are from 5,000 to 10,000 pellagrins in the United States. Furthermore, it has been established that the disease doubtless existed there for at least fifteen or twenty years and probably for thirty-five or forty years before it was recognized. It is interesting in this connection to note certain changes in vogue in recent years regarding the harvesting and marketing of maize in the United States, as pointed out by Nichols(12): Shelled maize is marketed from four to eight weeks earlier than formerly, the time of weathering and drying it on the stalk also is cut short, and more trouble is experienced in handling the maize and preventing it from spoiling. Sambon,(13) in 1905, after discussing the various theories of the zeists as to the etiology of pellagra, concluded by saying that if he were asked to suggest a new theory of pellagra he would feel inclined to draw attention to the many analogies between it and some of the protozoan diseases. It has been claimed recently that the disease is caused by a protozoan(14) parasite transmitted to man by a minute biting midge of the genus *Simulium*. The protozoan theory is, at present, attracting much attention. Taylor(19) draws a striking comparison between the points of similarity occurring in pellagra, sleeping sickness and syphilis. However, the results secured by applying the Wassermann reaction to pellagrins are conflicting. Bass(1) obtained 8 positive reactions out of 12 cases, other conditions, such as syphilitic history, malaria, etc., which might have had their influence, being excluded. Fox,(3) on the other hand, obtained three or four weak reactions, but not a single strong positive one in 30 cases. However, he used Noguchi's modification of the Wassermann test.

The following conservative resolution was adopted at the closing session of the conference on pellagra, held at Columbia, South Carolina, November 3 to 4, 1909.

"*Resolved*, That while sound corn is in no way connected with pellagra, evidences of the relation between the use of spoiled corn and the prevalence of pellagra seem so apparent that we advise continued and systematic study of the subject and, in the meantime, we commend to corn growers the great importance of fully maturing corn on the stalk before cutting same."

Although individuals of all ages are susceptible to pellagra, the majority of cases occur in persons between 20 and 50 years of age. Locality predisposes only in so far as the climate may be favorable for the growing and maturing of corn. Other conditions have no predisposing influence except as the general state of nutrition may be lowered thereby. Direct sunlight is not necessary for the production of typical skin lesions of pellagra, though they may be influenced somewhat by it. Lombrosso, to some extent, controlled the location of lesions by the use of fenestrated gloves, but it is shown that gipsy children of Roumania, who go about naked, have skin lesions of pellagra confined to the usual sites (Neusser),[9] and five of Walker's(23) cases had not been out of doors in eight months.

The pathologic findings are neither constant nor characteristic, and Harris(5) says that "there are few, if any, diseases characterized by perceptible organic lesions the pathological anatomy of which is so difficult to arrive at as that of pellagra." The evidences of cachexia are seen in the wasted muscular tissue and in the atrophic and fatty changes in the heart, lungs, liver, kidneys, and spleen. In the digestive tract, the tongue is more or less denuded of epithelium, the gums and the buccal mucosa are the seat of a dirty, grayish deposit and perhaps of ulceration, the mucosa of the stomach is frequently hyperæmic, especially at the pyloric end, and slight areas of hyperæmia are found in various locations in the large and small intestine. Ulcerations also may occur and in various situations there usually is found a thinness of the walls of the intestine. When examined microscopically, this is found to be in the muscular tissue. In performing the autopsies, one is impressed with the slight pathologic changes in the digestive tract as compared with the marked symptoms which often precede death.

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[9] Quoted by Sambon.

Tuczeh[10] calls attention to abnormal pigmentation in the ganglionic cells, heart musculature, hepatic cells and spleen. He believes that the hyperæmia, anæmia, œdema and, at times, inflammatory affections of the central nervous system and its coverings, together with the obliteration of the central canal of the spinal cord, are not peculiar to pellagra, but are present in many chronic affections of the central nervous system and in senility. Other findings in the brain are negative, except for fatty degeneration or calcification of the intima of small blood vessels and pigmentation in the adventitial coats. However, in the cord, Tuczeh[11] found fairly constant and important changes, namely, a degeneration in the lateral columns in the dorsal region and in the posterior columns in the cervical and dorsal regions, with very few changes in the lumbar region. Lombrosso[12] confirmed these findings, as did Sandwith,(16) but they believed the lesions of the posterior columns to have originated in the posterior nerve roots. Harris(5) found a combined sclerosis and from the character of the lesions was led to discredit the occurrence of so-called acute pellagra, believing that practically all cases are chronic and die when suffering from an acute exacerbation.

The skin changes usually consist of congestion, thickening and pigmentation, and atrophic thinness. (Radcliffe-Crocker.)[13]

The alterations in the blood, other than a secondary anæmia, are inconstant. Relatively large mononuclear increase has been reported. In a few of Walker's(23) cases the hæmoglobin varied from 65 to 95 per cent, red cells from 2,500,000 to 5,292,000, whereas the white cells showed but slight and inconstant variations. Nucleated red blood cells were found in three out of ten cases and were present early in the disease and when the hæmoglobin was either normal or above that figure.

To sum up, aside from the changes in the skin and those to be expected in a general cachectic condition, practically the only constant pathologic findings are those in the spinal cord.

The attempt to discover prodromal symptoms has been unsatisfactory for the reason that the great majority of cases in Europe have occurred among the poorer agricultural classes, who are accustomed to pay but little attention to the lesser ills of life, as well as to the fact that most of the cases in the United States have been studied in insane institutions.

One of my cases, a white female, recovered sufficiently to give a fairly good history. The first symptoms which attracted her attention were slight vertigo, insomnia, an increased appetite, irritability, occipital headache, lassitude, a growing lack of interest in her home and family, slight irregularity in her bowel movements (chiefly of a diarrhœal nature), difficulty in remembering names, and a vague fear that some calamity would befall her. She did not recall having nausea, a burning sensation in the stomach, or abdominal pain particularly referred to the epigastric region, symptoms mentioned by various writers as prodromal of the disease.

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[10] Quoted by Lavinder.

[11] Quoted by Sandwith.

[12] Quoted by Sandwith.

[13] Quoted by Lavinder.

When pellagra is well established, the symptoms fall into three groups, skin lesions, digestive symptoms, and nervous and mental manifestations.

The skin lesions are symmetrical in distribution and involve chiefly, almost exclusively, the uncovered portions of the body: the hands, feet, face and neck. The elbows frequently are involved and lesions in unusual locations are reported: For instance, Walker had two cases in which the nipples were attacked and one case in which the umbilicus was affected. The extensor surfaces of the hands and feet are involved primarily; the palmar and plantar usually are not affected. The first appearance of the lesions generally is erythematous, but initial erythema may be lacking (Lavinder) (7). The erythema not infrequently is accompanied by some local puffiness and a sensation of burning, the whole picture being somewhat like sunburn. D'Oleggio believed the condition to be caused by the sunlight and as the lesions in Italy, at least, tend to recur in the springtime, he called it *vernal insolation*, the popular name being *mal de sole.*

Vesicles and bullæ which easily become infected may follow the erythema and these, upon breaking down, disclose a raw, weeping, and at times ulcerated surface. In other cases, the skin dries and desquamates, leaving a slightly pigmented surface, or possibly a normally appearing skin. However, initially the skin may be dry, rather thick and pigmented to a bronze or blackish color. As the attacks are repeated, a chronic thickening and an increase in the pigmentation occur in the affected parts. The majority of writers believe that there is no relation between the severity of the skin lesions and the constitutional disturbance, while others consider the moist variety of lesion to be a grave symptom.

In the digestive tract, stomatitis is present in a large percentage of cases. The edges and under surface of the tongue, the floor of the mouth and the inside of the cheeks usually are reddened and the tongue may later appear to have lost its epithelium, constituting the so-called "bald" tongue. A whitish pellicle frequently is present upon the lower gum and this may involve all the mucous membrane of the buccal cavity. Its first appearance not rarely is back of the last molar tooth. Abdominal distress, a burning sensation in the stomach, nausea and vomiting may be present. Diarrhœa is the rule, but there may be constipation. The diarrhœal stools are characteristically of a light yellow or greenish-yellow color, they have a very offensive odor and a decidedly acid reaction, are often of a mushy consistency and, as a rule, vary in frequency from 2 to 6 a day. When other symptoms are well marked and great emaciation is present, the diarrhœa at times may give place to constipation, a condition which the physicians at the Georgia State Sanitarium have learned to regard with apprehension.

The nervous symptoms are very variable, depending upon the stage of the disease and the individual case. The earliest symptoms are headache, restless irritability, insomnia (rarely drowsiness), vague neuralgias and some depression of spirits. As the disease advances, these symptoms become more marked and an alteration in the knee jerk occurs. In some cases, with mental symptoms similar to those of acute mania, all of the deep reflexes appear to be increased. Muscular weakness is characteristic. Many other conditions of a miscellaneous nature are reported, such as paraplegia, hemiplegia, contractures of the extremities, tetanoid states, convulsions, tremor of the tongue, head and upper extremities, and paræsthesias. Trophic changes also, such as œdema, sensations of cold, and general paleness, are reported.

Some cases show no mental involvement, while others vary from slow cerebration, faulty memory and slight depression, to asylum cases where almost any psychosis from dementia præcox to senility may be simulated. Some, with a history of long-continued illness, are diagnosed readily as an infective-exhaustive type, but others may be confused with manic-depressive insanity in the depressed stage, involutional melancholia, imbecility or dementia præcox. Negative symptoms, particularly with regard to taking food, not infrequently are present, and also stereotyped movements. Bizarre, fantastic, changeable delusions, often of the nature of a phobia, are at times coupled with a profound depression. As in the case of skin lesions, where a slight change is left in the affected parts when one attack clears up, just so some depression, irritability, and lack of interest in ordinary duties is left over, and as often as the disease recurs this condition is increased.

Many of the insane in Italy are pellagrins. There were 945 such cases in 1874, and 1,348 in 1877. Statistics for Saint Clement's Hospital of Venice give the following data (King) (6):

	Number of insane.	Pellagrous insane.
1874	558	178
1875	595	158
1876	666	175
1877	802	215
1878	859	294
1879	924	337

It is not stated whether these pellagrins were insane when admitted to the hospital or became pellagrous after admission.

A vaginitis is quite common in the genito-urinary tract, occurring about the same time as the skin lesions and the stomatitis. Coupled with these various symptoms there is an increasing emaciation as the pellagra recurs from year to year, until finally the patient dies of exhaustion or some intercurrent disease.

While nearly all of the old-world cases are of the chronic type just described, there are records of acute ones (Lavinder)(7). Walker(23) reports 51 cases of so-called acute pellagra in the United States; Searcy(17) 88 of epidemic acute pellagra, and Zeller(27), of Illinois, 130. Harris(5) is inclined to believe that all cases are chronic because of the nature of the pathologic lesions in the spinal cord, even of those who died in an apparently acute attack. In this connection it is interesting to note that Siler(18) found that many of the Illinois series gave a history of preceding attacks, whereas 80 per cent of Searcy's(17) were previously in good health. Certainly, there is a wide divergence clinically between the cases clearly chronic, recurring yearly, and those apparently acute, which, without giving a history of a preceding attack, terminate fatally in from about one week to two months.

The various symptoms of pellagra develop quickly and are severe in these rapidly fatal cases. The development of stomatitis, skin lesions, and digestive disorders in which vomiting is not uncommon and diarrhœa is persistent, leading to rapid emaciation, pronounced nervous and mental manifestations, vaginitis, slight fever and the occurrence of bedsores, is so rapid that the picture is rather explosive in character when compared with typically chronic cases which continue for years.

The division of pellagra into varieties depends upon the symptoms which are most pronounced. On this basis, the following division is given (Procopin):[14] (1) gastro-intestinal; (2) nervous, with mania; (3) nervous, with paralysis; (4) *pellagra sine pellagra;* and (5) typhoid pellagra.

Some authors discredit the occurrence of *pellagra sine pellagra,* and doubtless it is true that this division affords a good opportunity for other affections to be diagnosed as pellagra. There is no symptom more characteristic of pellagra than the skin lesions. However, I have seen at least one case in which the lesions were very slight and fleeting in character. In 8 per cent of Searcy's(17) series the cutaneous system was not involved. In the typhoid variety, a typhoid state has developed, but the *Bacillus typhosus* is absent.

The diagnosis of a well-marked case which exhibits the typical skin lesions, stomatitis, diarrhœa and depression is made easily after the physician has once seen pellagra. As in other affections, the atypical cases offer difficulties. A history of maize eating is important. In my opinion, the strongest evidence of pellagra is found in the skin lesions, and in the absence of this symptom one should be cautious in rendering a diagnosis. The London School of Tropical Medicine instructs its students to diagnose pellagra before the skin lesions appear, and certainly it would be well if diagnosis could be rendered thus early in all cases. However, as stated before, the division of *pellagra sine pellagra* affords an opportunity for incorrect conclusions to be drawn. Recently, I have read the reports of two or three cases of pellagra which, in my opinion, were not pellagra at all. Provisional diagnosis could be rendered in such instances and time would indicate the positive diagnosis.

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[14] Quoted by Lavinder.

The prognosis is guarded, even though the patient may recover from one attack. The most hopeful cases are those of the chronic type without mental involvement; the least so, those of the acute or fulminating variety with pronounced mental impairment. Searcy says that the majority of acute cases die within from ten days to six weeks after the onset. The chronic ones recur in increasing severity year after year and the patient finally dies of exhaustion, or of an intercurrent disease. Some affections are said to have continued for twenty-five years.

Fever, marked mental symptoms, and a typhoid state are looked upon with gravity, as also is any complication.

Lombrosso, in 1884, found that 13 per cent of a large number of cases died. (Lavinder.) The death rate in Italy in 1905 was 4 per cent.(26) Of the cases at the Peoria State Hospital, Illinois, 22 per cent died, 10 per cent were not expected to recover, 17 per cent improved, and 51 per cent apparently had recovered, when reported. (Siler.) (18)

Italy especially has instituted prophylactic measures against pellagra, all her efforts being directed against the use of spoiled maize as food. The Italian law of 1902 regarding the prevention and cure of pellagra provides for a census of the disease and a report of all new cases; artificial dessicating plants and public storehouses for maize; exchanges where, under certain conditions, good maize is given for spoiled; the exclusion from entrance into the country of spoiled grain and the inspection of home-grown maize when brought to the mill; the education of the public, including the school children, by means of lectures and pamphlets as to the causation and prevention of pellagra; and farmers' institutes to teach the peasantry better methods of agriculture. Apparently, the measures have been very successful, as indicated by the fact that in 1906, 1907, and 1908 the new cases reported were, respectively, 6,783, 5,307, and 2,766. (Wollenberg.) (26) However, it is pointed out that this decrease in the number of new cases is coincident with an improvement in general conditions in Italy; that emigration has reflexly widened the view of the peasant class so that they demand and get better food and living conditions; that wages are higher and that the consumption of meat is increasing. (Lavinder.) (9)

The law of 1902 provides, as curative measures, for the establishment of rural bakeries from which well-made, wheaten bread is distributed to those ill of pellagra, and also hospitals (*pellagrossari*) for the treatment of the more pronounced cases of the disease. There are now 22 such hospitals in Italy. (Thayer.) (20) The patients are given a liberal diet and are treated symptomatically, slight importance being placed on any one drug; and these efforts appear to be successful, since in 1906 and 1907 the death rate from pellagra in Italy fell to about one-fifth of the former death rate. (Wollenberg.) (26)

Austria, in 1905, provided for its pellagrins by establishing community bakeries where bread from fresh flour was distributed, each patient receiving daily a loaf weighing 1 kilo; salt and meat were given for a period of from sixteen to forty weeks; free pamphlets relating to the cause and prevention of the disease were circulated, with the result that 86 per cent of the patients were benefited to such an extent that they could attend to their ordinary duties even in cases where the disease was of from four to eight years' duration. In 1909 there were recurrences in 126 of the cases treated during 1907 and 1908. (Vienna letters.) (21, 22)

No drug has been found to counteract pellagra. The best results, as just indicated, have been obtained by excluding corn from the diet, giving a liberal allowance including meats, and treating the cases symptomatically. Tonics are often administered. The skin lesions do not respond well to local treatment. The exhibition of common salt is thought to be beneficial. Arsenic in the form of Fowler's solution, arsenic trioxide, atoxyl and soamin has been used, but reports of the results are very conflicting, some men apparently obtaining good results, while others believe that no beneficial effects are secured from its use. However, the balance of evidence tends to show that Fowler's solution is of importance, especially in nonasylum cases. Reports regarding the administration of atoxyl and arsenic trioxide combined have recently been made and encouraging results claimed (Babes),[15] but these have not been verified.

Bearing in mind that pellagra is a disease which characteristically recurs, it is evident that the physician must be exceedingly careful in interpreting apparently *good results* from the use of any drug. Warnock,[16] in 1907, believed atoxyl had a favorable action, but, in the following year, he lost faith in its beneficial effects (possibly because of recurrences).

There is evidence tending to show that specific antibodies are developed in the blood, and the serum of cured cases has been used successfully in the treatment of typhoid pellagra (Antonini and Mariani).[17] Cole and Winthrop (2) report successful results in 6 out of 9 cases treated by transfusion. In some of the cases the blood of a cured pellagrin was used, but in most of them the blood was taken from a healthy individual. Special reasons existed why the operation would probably be unsuccessful in the three which were fatal.

PELLAGRA IN THE PHILIPPINE ISLANDS.

Mariano Agustin, of Cabeceria No. 10, of San Antonio, a hacienda of the Compañia Tabacalera, and a barrio of Ilagan, Province of Isabela, an Ilocano, was born in Batac, Ilocos Norte. He moved to San Antonio about fifteen years ago. He is about 30 years of age and the father of three healthy children, the youngest of whom is between 3 and 4 years old. Since moving to San Antonio, he has continuously lived in that place and been engaged in growing tobacco. His family history is negative except that his father died suddenly two years ago at about 60 years of age. No history of serious illness could be elicited until the present illness began. The patient says his chief articles of diet have been maize, grown at San Antonio, and rice, but largely maize.

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[15] Quoted by Lavinder. [16] Quoted by Lavinder. [17] Quoted by Lavinder.

Somewhat more than two years ago the patient had attacks of diarrhœa alternating with constipation. The diarrhœal stools were of a mushy consistency, light yellow in color, and varied in number from two to six a day. About the time the diarrhœa developed, the skin of the extensor surfaces of the hands and feet became rather thick and pigmented, and the forearms, legs, thighs and buttocks were affected with a different kind of a dermatitis. Previously, his neck had become enlarged anteriorly. It was impossible to determine whether the hands and feet were reddened at first or whether the lesions were at any time moist.

While the patient says his hands and feet have been continuously pigmented since the eruption first appeared, his answers to certain questions tend to show that there have been three exacerbations or recurrences in his symptoms. He refuses to take a bath, except by having the water poured on his head, because his symptoms were more pronounced on one occasion after having taken a bath in the usual way; he also, for similar reasons, refuses to have his hair cut and his nails trimmed.

Throughout this period the patient has slept well and has had a good appetite, but has felt that he was growing weaker. In January, 1910, there were some skin lesions on his face. He realizes that he has become irritable and depressed. He has not walked for several months.

The patient is a fairly well nourished man of above medium height. His arms, and especially his legs, are diminished in size; the muscles are flabby. He complains of nothing but weakness. His countenance indicates mental depression, and this, together with his long hair and nails, a peculiar dermatitis involving the hands and feet symmetrically and an enlarged neck, probably from goiter, gives him a rather striking appearance.

A dry, rather thick, blackish, somewhat granular dermatitis involves the extensor surface of the hands quite symmetrically, and fades away rather abruptly slightly above the wrist joint; this gives place to a dermatitis which extends nearly to the elbow, involves the whole circumference of the forearm and is characterized by large, thin, grayish-colored flakes. At the wrist joint the first variety of determatitis spoken of extends around the forearms like a bracelet. The feet are affected in precisely the same manner as the hands and with precisely the same sort of dermatitis; it fades away rather gradually above the ankle joint to give rise to the large, flaky variety of dermatitis which involves not only the legs, but also the thighs and buttocks. This is more pronounced on the lower than on the upper extremities. Both varieties of dermatitis are symmetrical in distribution. The palmar and plantar surfaces are not involved. Slight puffiness of the extensor surfaces of the fingers is present. No burning sensation of the affected parts is experienced by the patient, but he complains of some itching wherever dermatitis is found.

Unfortunately, the patient's mouth was not examined, but he stated that his mouth was not at the time, and had not been, sore. Examination of the abdomen is negative, as is that of the lungs, but the heart is found to be enlarged, the apex beat being displaced outward and downward. No murmurs. The examination of the nervous system is unsatisfactory because it is impossible for the patient to understand what is desired. However, fine tremors of the upper extremities are present, the knee jerks appear to be diminished and the Babinski reflex is absent. Mentally, the patient is at times irritable and moody, but usually he is depressed and indifferent to what is going on around him. His answers to questions are slow, as though he had difficulty in finding words to express himself, and he apparently entertains vague fears that some ill will befall him. Memory for recent events is good. He has no hope of recovery. Pulse full, regular, 68 per minute. No capillary pulse, exophthalmos absent; temperature normal.

Facilities were not at hand for examining the blood or the urine, but the latter was apparently normal as to color, amount, and frequency. The fæces were light yellowish, soft, decidedly acid in reaction and negative for evidences of parasitism.

The patient was in about the same condition each time he was seen, and the above notes were taken from the results of examinations during five visits. He was told to abstain from eating maize and rice but that he might eat all he desired of other things, especially eggs, chickens and milk. He was also given elixir of iron, quinine and strychnine. The directions were not followed either as to diet or the tonic.

Having had the opportunity of seeing a number of cases of pellagra in the Georgia State Sanitarium during the past two years, I believe the case here reported to be one of that disease. The involvement of the hands and feet, the character of the bowel movements and the depression, cardinal symptoms of pellagra, all form a very striking picture. However, because of the impossibility of obtaining a perfectly accurate history either from the patient or his family, because of the presence of the second variety of dermatitis, which is new to me (but which is not uncommon at San Antonio), and because of the fact that pellagra has not yet been reported from the Philippine Islands, the diagnosis is modified to a case of probable pellagra.

It is well known that in certain parts of the Philippine Islands maize forms the chief article of diet. This is true of the tobacco districts of the Cagayan Valley, and among certain wild tribes (e. g., Negritos), in Bulacan and Pampanga Provinces. Since pellagra is found in so many parts of the world where maize is cultivated and used as a foodstuff, and it seems so apparent that the cause of pellagra is in some way connected with the eating of maize, one would rather expect to find the disease in the Philippine Islands. It may be added that several physicians have told me that certain cases seen by them may have been pellagrous. Dr. Cesar Sorcrain, of Ilagan, tells me he has seen eight cases of pellagra during about twenty-two years of practice in the Cagayan Valley.

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ILLUSTRATION.

Plate I. Case of probable pellagra.

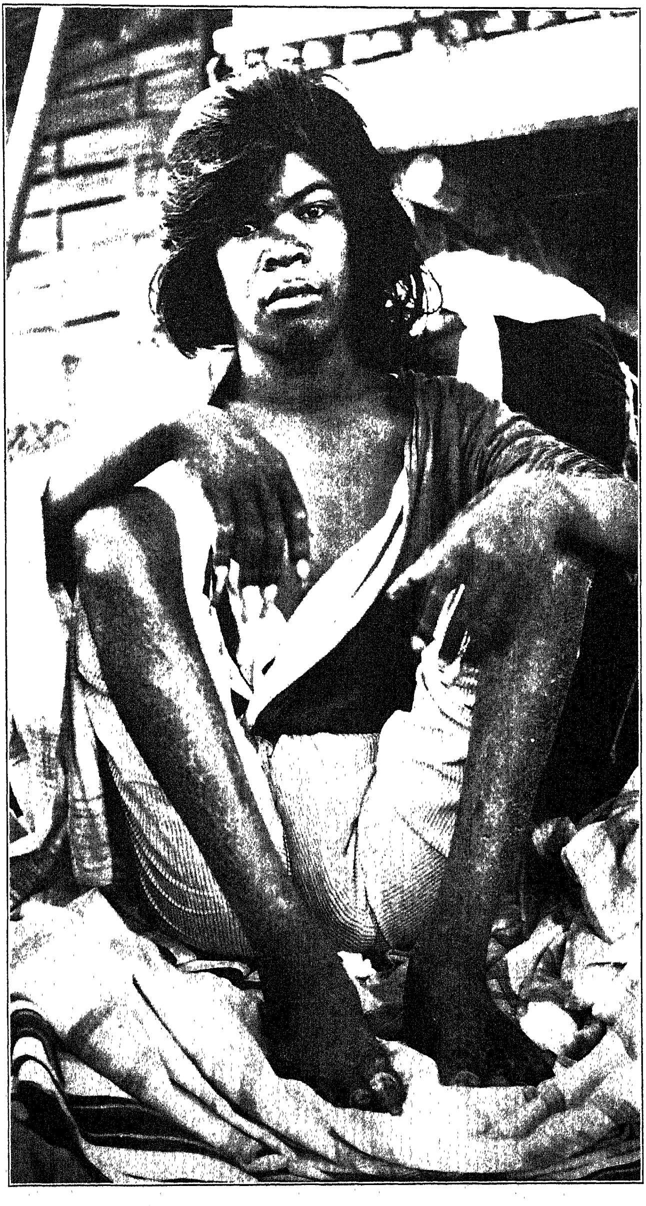

PLATE I.

EXAMINATIONS OF STOOLS AND BLOOD AMONG THE IGOROTS AT BAGUIO, PHILIPPINE ISLANDS.[1]

By W. P. Chamberlain, H. D. Bloombergh, and E. D. Kilbourne.[2]

THE IGOROT PEOPLE.

The Igorots, commonly thought of only as head-hunters, are the most remarkable of the wild tribes of the Philippines. Perhaps no savage people has so extensively and laboriously built up such a system of irrigation and intensive farming. In the deep valleys and cañons of the rugged mountain ranges of northern Luzon they have constructed their *sementeras* or terraces for the growing of rice and camotes, the latter a vegetable allied to the sweet potato. These terraces are rock faced, the surfaces are accurately leveled and diked, they are irrigated by water diverted from mountain streams and often carried in artificial channels for considerable distances. The agricultural works of these people equal or surpass those of the Japanese, with which many of us are more familiar. The most notable examples of terracing are in the subprovince of Ifugao and indicate that the Igorot possesses a high degree of engineering and constructive skill. They were driven by necessity to this high development in agriculture, owing to the rugged character of the country where subsistence on the natural products of the soil was impossible and where game and fish were relatively scarce.

There are supposed to be 183,000, perhaps even 225,000 Igorots, divided between many tribes, differing widely in customs, habits and dialects. (1) It is thought by some that they belong to the first of the primitive Malay tribes which invaded the Islands, displacing the aboriginal Negritos, and that later they were themselves driven to the refuge of the mountains by more warlike maritime invaders. They have been but little influenced by the Spanish civilization.

THE IGOROT COUNTRY.

The region occupied by this people, although well within the Tropics, possesses a temperate climate, the heat to be expected in low latitudes being modified by high altitude. The country is rugged, mountainous and well watered, with the rivers for the most part winding in deep gorges and cañons. It is practically devoid of lakes. The Igorots live at altitudes ranging from about 600 to 2,400 meters above the sea level. The Baguio plateau, where the summer capital of the Philippines is situated, has an elevation of about 1,500 meters. The mountains around Baguio are moderately wooded, the forests being of pine and in large part free from underbrush, but in some portions of the mountain provinces the character of the forests is more tropical.

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[1] Published with permission of the chief surgeon, Philippines Division.

[2] W. P. Chamberlain, major, Medical Corps, United States Army; H. D. Bloomberg and E. D. Kilbourne, captains, Medical Corps, United States Army, constituting the United States Army Board for the Study of Tropical Diseases as they exist in the Philippine Islands.

The rainfall in this section of Luzon is very great, being heaviest in July, August, and September. The mean annual fall over a period of eight years at Baguio was 371.1 centimeters. Baler in Luzon, Capiz in Panay, and Cherra Poonjee, a hill station in India, are the only places in the world with higher recorded rainfall. The warmest month is May and the coldest February. The highest recorded temperature at the Mirador Observatory in Baguio for eight years (1900–1908) was 29.3° C. and the lowest 3° C., while the mean maximum for May was 25.6° C. and mean minimum for February 7.5° C. These temperatures were taken about 3 meters above the earth. On the ground, as a result of nocturnal cooling or terrestrial radiation, the temperature occasionally falls low enough to congeal water in small puddles.

PHYSICAL CHARACTERISTICS OF THE IGOROTS.

The Benguet Igorots are a people of low or medium stature. Bean found the average height of 104 adult males to be 154 centimeters, and of ten adult females to be 146.7 centimeters. (2) The male is well built, rarely corpulent, and his symmetrical muscular development is remarkable, especially in the lower extremities. The legs of the female are both absolutely and relatively shorter than those of the male and the muscular development of the lower extremities so great as to cause them to appear clumsy. Deformities of the feet in both sexes are very common, especially an inward spreading of the great toe. In their physical development the Igorots contrast sharply with the poorly nourished and slightly built Negritos. Among the Igorots the men and women are upon a nearly equal footing and both act as field laborers and as *cargadores* (carriers) over the steep mountain trails. Men and women both age rapidly, especially the latter, who are shrunken and wrinkled hags when 40 to 45 years old.

The complexion of the Igorots is brown, of varying shades, sometimes appearing like bronze, and many of them resemble closely in appearance the American Indian. The hair is black, coarse and straight, rarely having a slight waviness. The Igorot is not cleanly either in habitation, person or clothing, in these last two respects contrasting unfavorably with many of the other Filipino tribes.

FOOD AND HABITS.

The food of the Igorot consists mainly of rice and camotes, the latter usually being planted in the same *sementera* after the rice is harvested. In some sections corn, beans and millet are grown, but rice is the staple food and is usually abundant in quantity, and the people are well fed and nourished. The half-cooked meat of carabaos, dogs, pigs and fowls is used to some extent, but usually in ceremonial feasts. The Igorots of Benguet, eat dogs only when the animals have become thin as a result of starvation, and in that province the consumption of these animals is considerable. The men are great smokers and drink a liquor made from fermented rice.

The Igorots live in small pueblos of a few hundred souls and for the most part their houses are low and provided with earth floors. The clothing of the men, after the age of puberty, consists of a breechcloth, often used only as an apron. They frequently carry a blanket to use as protection against the cold. The women wear a strip of bright-colored material arranged like a short skirt, reaching from waist to knee, but they frequently work in the fields entirely nude. In both sexes the feet are always bare and opportunities for infection with parasites through the skin while on the trail, in the village or in the rice field seem excellent. Doubtless the chances for infection *per os* with food, water and soiled hands are equally good. Since many of the Igorots go as *cargadores* to the lowlands, distant not over 20 miles from Baguio, some of the intestinal parasites they harbor may have been acquired there rather than in the hills.

EXAMINATIONS OF FÆCES.

During a visit to Baguio by two members of the Board for the Study of Tropical Diseases, an examination was made of stools and blood of 119 apparently healthy adult Igorot laborers. Of these 56 were working for the quartermaster at Camp John Hay and the remainder were employed by the Bureau of Public Works of the Civil Government.

In all the stool examinations three cover-glass preparations of fæces in each case were completely looked over before recording the results and in some instances where no ova were then found a still further search subsequently was made. By such a method we feel sure that we discovered the great majority of the vermicular infections, but undoubtedly even with this routine a few cases of mild uncinariasis were overlooked. No effort was made to find amœbæ since all of the specimens when received were several hours old and at a low temperature.

Among our 119 Igorots, 92.5 per cent of the whole had the ova of some intestinal parasite in the evacuations. *Ascaris lumbricoides* was the most commonly observed, 73 per cent of those examined showing eggs of this nematode. Next came *Trichocephalus dispar*, with an infection rate of 60 per cent, then Uncinaria with 29 per cent, and last of all *Tænia* with 12 per cent. Most of the men showed two varieties of parasites, many three, and a few harbored four kinds.

As it was impracticable to treat these natives, we were unable to determine the species of uncinaria present, but judging from experience elsewhere in the Philippines it is probable that it was in most cases *Necator americanus*. All of the tapeworm eggs appeared to be those of *Tænia saginata* except those from one man, whom we considered to be infected with the *Dipylidium caninum*, but here again we were unable to obtain the parasite to confirm the opinion based on the appearances of the ova.

TABLE I.—*Ova found in the stools of 119 male Igorot laborers examined by the Tropical Board at Baguio, P. I.*

Examinations and infections.	Number.	Per cent.
Persons examined	119	
Persons infected with intestinal parasites	110	92.5
Persons infected with—		
Ascaris lumbricoides	87	73.0
Trichocephalus dispar	72	60.0
Uncinaria	35	29.0
Tænia	15	12.0
Total number of infections	209	174.0

The total number of infections agrees closely with the findings at Taytay, where 95.9 per cent of the 1,000 Filipinos examined were infected.(3)

While at Baguio, through the courtesy of Doctor Vincent, we were permitted to study the records of stool examinations of Igorots at the Civil Hospital for the last two and a half years and we have arranged these data, for ease of reference, as shown in Table II.

TABLE II.—*Stool examination of 183 Igorots at Civil Hospital at Baguio, P. I., July 1, 1907, to March 3, 1910.*

Persons infected with—	Number, fiscal year—		Number to March 3, 1910.	Whole period.	
	1908	1909		Number.	Per cent.
Ascaris lumbricoides	10	14	25	49	26.3
Trichocephalus dispar	13	13	27	53	29.0
Agchylostomum	6	13	34	53	29.0
Tænia solium	3	2	0	5	2.7
Tænia saginata	0	0	4	4	2.4
Amœba	8	2	2	12	6.6
Trichomonas	0	0	1	1	0.6
Oxyuris vermicularis	0	0	4	4	2.2
Strongyloides	1	0	0	1	0.6
Distomum hepaticum	1	0	0	1	0.6
Total number of infections	42	44	97	183	100.0
Total number of persons examined	23	42	118	183	

There are no data to show how many of the entire 183 patients examined showed no parasites of any kind.

We do not know the individual age or sex of the 183 Igorots recorded at the Civil Hospital, but we are informed that 100 of them were school children under 15 years of age. The result of the examination of these 100 children is reported by Bowman in the Bulletin of the Manila Medical Society for April, 1910.(7) He found 56 per cent infected with some parasite, distributed as follows: *Ascaris lumbricoides*, 23 per cent; *Trichocephalus dispar*, 30 per cent; *Oxyuris vermicularis*, 13 per cent; *Agchylostomum duodenale*, 32 per cent; *Tænia saginata*, 2 per cent. This we take to mean that 32 per cent of the 56 infected school children were harboring hookworms, which would give 18 per cent of infection with uncinaria out of the whole series of 100 examined.

Comparing our finding with those at the Civil Hospital and with Bowman's results in children alone the following points are of interest:

1. We found a much higher percentage of vermicular infections, 174 per cent as against 100 per cent at the Civil Hospital.

2. We found 92.5 per cent of the men examined to be infected with some parasite, while Bowman encountered only 56 per cent of the school children infected. The percentage for the Civil Hospital is not known.

3. The difference in percentage between our findings and those by Bowman and at the Civil Hospital is due mainly to the fact that we encountered a very much greater number of infections with *Ascaris, Trichocephalus* and *Tænia,* as is shown graphically in the table.

4. The percentage of infections with uncinaria are the same in our series of adult males and in the combined Civil Hospital statistics, 29 per cent in each instance, but this is a much larger rate than was found among Bowman's school children, who gave 18 per cent.

This last difference is in line with observations made elsewhere in the Philippines. At Bilibid Prison and in Scout companies the rates of hookworm infection found among adult males has exceeded 50 per cent, while among 9,885 members of general population in Luzon examined by the Bureau of Health the infection rate has ranged from 11.1 to 16.1 per cent. In the general population when the statistics have been divided according to age and sex, the infection rate has been found highest in adult males, lower in women and lowest in children, as shown in the following table:

TABLE III.—*Shows percentages of hookworm infection among males, females, and children in Luzon.*

Place.	Number examined.	Per cent infected.		
		Males.	Females.	Children.
Taytay	1,000	[a]17.2	6.6	4.5
Las Piñas	6,000	24.0	8.0	------
Cagayan Valley	2,500	21.0	9.0	2.0

[a] For *adult* males the rate was 22.8 per cent.

4. The percentage of infections with *uncinaria* are the same in our

It will be observed that the percentages for males are not very markedly below that found for the Igorot laborers at Baguio.

As far as we could see on mere inspection, the Igorot men who were infected with uncinaria were little affected by the presence of the parasite. Bowman could find no relation existing between hookworm infection and the health of the children. This experience is in accord with observations made elsewhere in the Philippines and leads to the conclusion that uncinariasis is not the serious menace to the health and progress of the Filipino that it has been found to be in the case of the natives of Porto Rico and the white man in the southern part of the United States.

EXAMINATIONS OF BLOOD FOR PARASITES.

Examinations for *Filaria nocturna* were made on the blood of 100 adult male Igorots. The specimens were obtained between 9 and 11 o'clock p. m. in the form of a thick smear, the hæmoglobin was washed out and the preparations then searched for the parasite, with negative results in every case.

An examination of the blood of 6,400 inhabitants of the Philippine Islands by former members of this Board has given some idea of the prevalence of filariasis in different parts of the Philippines.(5) The disease appears to be of most frequent occurrence in Bohol, Leyte and especially the extreme southern end of Luzon where the infection rates among the natives range from 5 to 10 per cent. Northern Luzon showed rates ranging from 0.2 to 0.8 per cent. This is the first work done by the Board in the mountain regions of Benguet and Lepanto-Bontoc and, in so far as such a small number of examinations is of value, indicates that the disease is not frequent there. We saw no cases of elephantiasis among the Igorots.

The stained blood smears from 40 adult Igorot laborers were examined for the parasites of malaria, and none were found. Malarial organisms are common in the blood of Filipinos in the lowlands, even when no symptoms of the disease are manifest.(9) Their absence in the Igorot is in keeping with the observation of Bowman that no patients with malaria were found at Baguio whose infection could be definitely traced to that locality.(7)

DIFFERENTIAL COUNT OF LEUCOCYTES.

Differential counts of the leucocytes were made in smears from 40 of the men whose stools had been examined and the results of the blood count, correlated with the stool findings, are shown in the following table. Two hundred white cells were counted in each instance.

TABLE IV.—*Table showing ova found in fæces and differential counts of leucocytes in 40 adult Igorot laborers examined in Baguio, P. I.*

Case number.	Uncinaria.[a]	Trichocephalus dispar.[a]	Ascaris lumbricoides.[a]	Tænia.[a]	Polymorphonuclears.	Eosinophiles.	Lymphocytes.	Large mononuclears.	Transitionals.	Mast cells.
					Per ct.	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*
1	--------	--------	--------	--------	40.0	9.0	43.0	4.5	3.5	--------
2	+++	--------	--------	--------	49.5	14.5	34.5	--------	1.0	0.5
3	+++	+++	--------	--------	35.0	15.0	39.0	5.0	5.0	1.0
4	--------	+++	--------	--------	38.0	8.0	44.0	7.5	2.0	0.5
5	--------	++	--------	--------	52.0	4.0	38.0	1.5	3.5	1.0
6	+	--------	--------	+	55.0	14.0	25.0	4.0	2.0	--------
7	--------	++++	++++	--------	53.0	4.0	33.0	4.5	5.0	0.5
8	++	++	--------	--------	49.5	6.0	40.0	2.5	1.5	0.5
9	++++	++	++++	--------	64.0	17.0	15.0	1.0	3.0	--------
10	--------	--------	+	--------	57.0	11.0	24.0	8.0	--------	--------
11	++	++	--------	--------	60.0	--------	26.0	9.0	5.0	--------
12	--------	+	++++	--------	35.5	22.0	36.0	2.0	3.5	1.0
13	+	--------	--------	--------	50.0	14.0	30.0	6.0	--------	--------
14	--------	+	+	--------	48.0	2.5	40.0	4.0	5.5	--------
15	--------	+	--------	--------	60.0	2.0	31.5	3.0	3.5	--------
16	--------	+	--------	--------	43.0	4.5	44.5	2.5	4.0	1.5
17	--------	--------	++++	--------	53.0	11.0	25.0	11.0	--------	--------
18	--------	--------	++++	--------	30.5	14.5	49.0	2.0	4.0	--------
19	--------	+	++++	--------	39.5	1.5	51.5	3.5	3.5	0.5
20	--------	++	--------	--------	52.0	17.0	27.0	2.0	2.0	--------
21	--------	+	++++	--------	28.0	18.0	46.0	2.0	5.0	1.0
22	--------	+++	++++	--------	49.5	2.5	41.0	5.0	1.5	0.5
23	--------	+	++++	--------	53.0	3.0	40.0	3.0	1.0	--------
24	--------	--------	++++	--------	49.0	17.5	30.0	2.5	1.0	--------
25	+	++	++++	--------	45.0	10.5	42.5	0.5	1.5	--------
26	+	+	+	--------	47.5	8.5	40.0	--------	3.5	0.5
27	+	+++	--------	--------	47.5	8.0	39.0	2.5	3.0	--------
28	--------	--------	--------	--------	49.5	5.5	38.5	3.0	3.5	--------
29	--------	--------	++++	--------	58.0	5.0	33.0	1.5	2.5	--------
30	--------	--------	+	--------	42.0	10.5	35.0	6.0	4.0	2.5
31	--------	--------	--------	--------	52.0	4.0	38.0	--------	6.0	--------
32	--------	+	++++	--------	59.0	0.5	35.5	1.5	3.5	--------
33	--------	--------	++++	--------	39.5	6.5	49.0	2.0	3.0	--------
34	--------	--------	++++	--------	33.0	6.0	53.5	2.5	5.0	--------
35	--------	--------	++++	--------	47.0	4.5	39.0	3.0	6.0	0.5
36	--------	+	++++	--------	24.0	32.5	37.0	3.5	3.0	--------
37	--------	--------	++++	--------	44.5	4.0	48.5	0.5	2.5	--------
38	+	+	+	--------	49.0	7.0	31.0	9.0	4.0	--------
39	--------	+	++	--------	43.0	8.0	35.0	5.0	7.0	2.0
40	--------	+	--------	--------	51.0	1.0	40.5	2.5	3.0	1.5
Total	11	24	24	1	--------	--------	--------	--------	--------	--------
Averages for blood					46.9	8.9	37.2	3.5	3.2	0.4

[a] When two or three ova of a species were found in one cover-glass preparation the result was recorded +++. Four plus marks indicate a greater number than this. If two preparations were looked over before the first egg was found the record was ++. One plus mark indicates that none were found in the first two preparations examined.

A study of Table IV shows that in nearly all of the differential counts some abnormality was apparent. The most evident change is the increase in the percentage of eosinophiles, only 8 out of 40 giving counts below 4 per cent. The highest was 32.5 per cent, another was 22 per cent and 15 were over 10 per cent. The average of the whole series was 8.9 per cent. In the Medical Survey of Taytay(4) the eosinophilia in 129 differential counts of the blood of Filipinos was 11.2 per cent and in 64 white American soldiers in the United States with uncinariasis it was 8.5 per cent.(6)

This increase in eosinophiles is to be accounted for in rare instances, perhaps, by skin diseases, but in the vast majority of cases by the infections with intestinal parasites. However, an increase is not invariable in the latter condition. Case number 11, with uncinaria and *Trichocephalus* ova present, had no eosinophiles in 200 cells and 7 other cases with *Trichocephalus* or *Ascaris* or both, showed the eosinophiles less than 4 per cent. Case number 1 gave 9 per cent of eosinophiles and no ova of intestinal parasites, but it is quite probable that a more thorough search would have revealed a few hookworm eggs.

The next most noticeable abnormality is a marked decrease in the relative numbers of the polymorphonuclear neutrophiles, which averaged 46.9 per cent for the whole series. This is in part due to the increase in the eosinophiles and in part to an abnormally large percentage of small lymphocytes, the average for the series being 37.2 per cent.

Comparing this with the results of differential counts on Filipinos at Taytay there is agreement in character, although the changes from normal are more marked in our series as shown below:

TABLE V.—*Average differential counts.*

Place.	Polymorph-neutrophil.	Eosinophiles.	Lymphocytes.	Large mononuclears.	Transitionals.	Mast cells.
Baguio	46.9	8.9	37.2	3.5	3.2	0.4
Taytay	51.7	11.2	34.5	4.1	———	0.1

Therefore, we may look upon the Igorots (and probably upon most other Filipinos) as having a chronically increased percentage of eosinophiles and small lymphocytes with a corresponding decrease in the polymorphonuclear neutrophiles, which condition apparently does not injuriously affect their health. This disturbance of the normal proportions of different varieties of leucocytes is probable common to most primitive and semicivilized peoples in the Tropics and the relative reduction of the polymorphonuclear phagocytic elements possibly may be a factor in the low resistance which such races offer to certain infectious diseases.

The decrease of polymorphonuclear neutrophiles, combined with increase of small lymphocytes seems in some way to be related to tropical conditions, not only being present in natives, as shown above, but also developing in white men after a period of residence in the Philippines. Wickline, at Camp McGrath, Batangas, examined the blood of 104 newly arrived white soldiers in good health, on three occasions, at eight-month intervals, and found a progressive decrease in the polymorphonuclears (64.4 per cent, 60.4 per cent, 54.8 per cent) and a steady increase in the small lymphocytes (21.8 per cent, 26.6 per cent, 33.3 per cent) and eosinophiles (4.1 per cent, 4.4 per cent, 5.1 per cent). That this condition of lymphocyte increase is not the direct result of helminthiasis is shown by the results of differential counts on 100 soldiers in New Orleans, Louisiana, 60 of whom had uncinariasis. In this series the polymorphonuclear neutrophiles were slightly diminished, 57 per cent, but this could be accounted for by the eosinophilia of 8.5 per cent. The lymphocytes were not above normal, averaging 27 per cent for the entire 100 men and 26.3 per cent for the 60 infected with uncinaria.(6)

During the experiments and observations with orange-red underwear, recently conducted by this Board, 445 differential leucocyte counts were made during a year on 115 healthy soldiers, the averages for the group being polymorphonuclear neutrophiles 56.3 per cent, small lymphocytes 34.7 per cent, large mononuclears 5.4 per cent, eosinophiles 2.8 per cent, mast cells 0.7 per cent. All of these men had been one or more years in the Philippines and show deviations from the normal, in the direction of lymphocyte increase and polymorphonuclear decrease, similar to those which developed in Captain Wickline's series. Neither in this work nor in Captain Wickline's observations was there found any abnormality in the absolute number of leucocytes per cubic millimeter of blood.

CONCLUSIONS.

(1) The Igorots are an industrious, well-developed and vigorous people, living in a climate comparatively temperate.

(2) Ninety-two and one-half per cent of 119 adult males examined showed ova of some intestinal worm in the stools.

(3) The infection rate with uncinaria among adult males was 29 per cent, which is probably higher than the average for the same class among the lowland Filipinos.

(4) The hookworm rate for children is lower, about 18 per cent.

(5) Malaria and filariasis are infrequent or absent.

(6) The blood shows a chronic condition of increased percentage of eosinophiles and small lymphocytes with diminished percentage of polymorphonuclear neutrophiles.

(7) The increase of lymphocytes and diminution of polymorphonuclears seems to be dependent on tropical conditions and will develop in white men living in the Philippines.

(8) This reduction in the number of polymorphonuclear phagocytic elements in the blood is both relative and absolute and may possibly be a factor in the lowered resistance to certain infectious diseases seen in tropical peoples.

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UNIDENTIFIED LARVÆ OF SOME DIPTEROUS INSECT DEVELOPING IN THE DEEP URETHRA AND BLADDER OF MAN PRODUCING SEVERE ABDOMINAL SYMPTOMS.[1]

By G. P. TRIBLE.[2]

Francisco José, a civilian employed at the United States naval station, Olongapo, Philippine Islands, reported to the sick quarters for treatment February 10, 1910, complaining of abdominal cramps. During that night the pain subsided and he slept well. The following morning the abdominal pain became very severe, accompanied with nausea, vomiting, and general abdominal rigidity. His bowels were open; urine was voided at 8 o'clock in the morning.

The patient was transferred to the U. S. steamer *Relief* at 3 o'clock in the afternoon. Upon admission his temperature registered 36.3° and general abdominal rigidity which was board-like over the bladder was present. Pain and tenderness were felt over the bladder and stomach.

A sterile, hard-rubber catheter was passed into the bladder, meeting some yielding obstruction in the deep urethra. About 150 cubic centimeters of clear urine were withdrawn. This contained numerous, actively motile, larvæ-like organisms. An examination of the fæces was negative. The urethra and bladder were then thoroughly irrigated with potassium permanganate and boric acid solutions. At 7 o'clock in the evening the symptoms had subsided to those of a mild case of acute cystitis. Two hundred cubic centimeters of urine were withdrawn, containing a few dead, but no living organisms. The patient complained of exquisite tenderness on passing the catheter through the deep urethra and sphincter.

Two days later all signs of bladder irritation had disappeared, the urine passed was clear and free from larvæ. The patient was discharged and returned to duty February 14, 1910.

In this case there was no history of disease of the urethra or rectum prior to the onset of the symptoms on February 11. The anterior urethra was normal. The eggs evidently were deposited and developed in the deep urethra, the larvæ passing through the sphincter of the bladder and causing acute inflammation of the bladder.

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[1] Read at the First Biennial Meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 7, 1910.

[2] Assistant surgeon, United States Navy.

DISCUSSION.

DISCUSSION OF THE PAPER "UNIDENTIFIED LARVÆ OF SOME DIPTEROUS INSECT DEVELOPING IN THE DEEP URETHRA AND BLADDER OF MAN PRODUCING SEVERE ABDOMINAL SYMPTOMS," BY DR. G. P. TRIBLE, ASSISTANT SURGEON, UNITED STATES NAVY.

Dr. E. R. Stitt, surgeon, United States Navy, associate professor of medical zoölogy, department of tropical medicine, Philippine Medical School, Manila, P. I.—A very interesting point in connection with the case reported by Doctor Trible is that of the identity of the larvæ. Those sent to me by Doctor Trible were not full-grown and there was some distortion. However, they resembled the larvæ of *Musca domestica.* I took some bottles containing horse manure and placed several females of *M. domestica* in them. The larvæ which developed agreed in all important details with those sent by Doctor Trible, an opinion with which Mr. Banks coincided, so that I think they were undoubetedly larvæ of *Musca domestica,* but the question is: How did they get into the urethra?

Mr. Charles S. Banks, Biological Laboratory, Bureau of Science, lecturer on medical entomology, department of tropical medicine, Philippine Medical School, Manila, P. I.—The question of how these larvæ got into the bladder is a very obscure and interesting one. They have no mouths in the sense that chewing larvæ have, namely coleopterous and lepidopterous larvæ. They get their food by means of two hooks which they use as scraping instruments, and by moistening with saliva the substances on which they live, they obtain a liquid diet, as it were. If this man had swallowed the ova or larvæ of the house fly, it is almost inconceivable that they could have traveled from the alimentary canal into the bladder. I have thought of this question considerably since Doctor Stitt mentioned it to me, and the only possible way I can see for this man to have become infected with these larvæ is by his having used some infected fluid for making a surreptitious injection. Larvæ of this class penetrate readily into any available cavity where they find suitable conditions for development, and thus they might have entered the external ureter and fixed themselves on the mucosa of the urethra.

Doctor Stitt.—I would like to say that the catheter used in this case was sterilized. It was taken directly out of the sterilizer and used at once; thus it was impossible for the infection to have occurred from this source.

Mr. Banks.—I do not want to be misunderstood or to convey the idea that there was any chance for infection while the man was being operated upon by a person in authority, but merely that the infection was probably caused by the man using some substance infested with the ova or larvæ of the fly and at a time and place unknown to the medical officer.

Dr. J. M. Atkinson, principal medical officer, Hongkong, delegate from the government of Hongkong.—These larvæ have been found in the stools of the Chinese. How they can enter the mouth and not be destroyed by the gastric and other juices met with in the intestinal tract is remarkable. They have been found by Doctor Bell in stools at the civil hospital at Hongkong.

REPORT ON THE CASE OF SUSPECTED HYDROPHOBIA IN A DOG, REFERRED TO IN THE PAPER BY DOCTORS DUDLEY AND WHITMORE, ENTITLED "HYDROPHOBIA IN THE PHILIPPINES."

MANILA, P. I., *July 9, 1907.*

The DIRECTOR OF SCIENCE, *Manila.*

SIR: I have the honor to inform you of the result of the inoculation of the material of suspected hydrophobia (medulla oblongata of a dog with the suspicion of Lyssa). The result shows it apparently to have been a real case. This assumption must be proved scientifically by further experiments.

On June 8, in the morning, the body of a dog, with suspected hydrophobia, was brought to my laboratory by Doctors Ashburn and Craig. I opened the scalp and took out the brain, and dissecting out the lateral ventricles of both sides, made 20 smears of the hypocampus for Doctors Ashburn and Craig, who examined the smears by staining with Azur II, and Azur-eosin stains (Giemsa's fluid) and stated that they found some bodies in contour like Negri's in them. I made the emulsion of the medulla oblongata according to the regular method and performed subdural inoculation through the foramen opticum into three rabbits. The following table shows the results:

Rabbit inoculation of suspected street virus, Manila.

Rabbits.	Inoculation.	Duration, days.	Date of death.	Source and symptoms.
No. 127	June 8	22	June 29	Slightly typical.
No. 128	do	24	July 1	Typical.
No. 129	do	31	July 9[a]	Do.

[a] Almost dying.

In Japan the incubation period of rabbits inoculated with street virus is about two weeks at a minimum, but sometimes in other countries, because of its weak virulence, we obtain the symptoms only in three to six weeks after the inoculation, which of course must be subdural. The result recorded in my table shows that the material was not contaminated with other septic bacteria and the assumption is that this was a real case of hydrophobia.

In rabbit No. 127 the symptoms were slightly typical, so I took out the brain, preserved it in sterilized glycerine solution and waited for the appearance of the symptoms among the other two rabbits. The second rabbit (No. 128) showed slight symptoms on the 30th of June and these developed on July 1 (next morning) into the typical form of this disease. The animal was nearly dead, when I chloroformed it and took out the brain, preserved it in Zenker's fluid, for a pathological examination by Doctors Ashburn and Craig. I injected the emulsion of the medula oblongata into three other rabbits. The spinal cords of both rabbits mentioned above I preserved in a vacuum to get material for injection by the Pasteur method of immunization.

I will now obtain the brain of the third rabbit and have smear examinations made by Doctor Ashburn, and on the other hand, with this spinal cord material, I will make inoculations into other rabbits. I have also performed subdural inoculation with the preserved material from the first rabbit.

For a long time, the existence of hydrophobia in the Islands has been under discussion and therefore we need perfect and exact investigation. We need, further, experiment and observation to prove the existence of this disease. Subdural inoculation must be made into a dog and the symptoms developed must be watched. I will have the honor to report as soon as my observations are completed.

Yours respectfully,

Y. K. Ohno,

Assistant in the Biological Laboratory, Bureau of Science.

REVIEWS.

Hookworm Disease. Etiology, Pathology, Diagnosis, Prognosis, Prophylaxis, and Treatment. By George Dock, A. M., M. D., and Charles C. Bass, M. D. Cloth. Pp. 250, 49 special illustrations and colored plate. St. Louis: C. V. Mosby Company. 1910.

Since it became evident about eight years ago that uncinariasis was common in the United States, many articles have appeared in American medical literature covering various phases of the subject. Important experimental work at the same time has been done on the disease in other parts of the world. The authors of this book show an intimate acquaintance not only with the literature of the subject, but also with the disease itself, particularly as it is found in the South Atlantic States. In addition, considerable research work has been done by them, especially in regard to the diagnosis of very mild cases (in which a centrifuge is used), in regard to the symptomatology of mild cases, and also as to the blood findings in the affection.

The subject of hookworm disease is brought quite up to date and the book, which is very appropriately dedicated to Dr. Charles Wardell Stiles, must find a hearty welcome among practitioners and medical students in the United States at this time when a crusade against uncinariasis has just been inaugurated.

The book is faulty in regard to the editing of technical names. It is unfortunate that the proof was not read by a zoölogist.

D. G. W.

Practical Suggestions In Borderland Surgery For The Use Of Students And Practitioners. By Gustavus M. Blech, M. D. Cloth. Pp. 219. Philadelphia: Professional Publishing Company. 1910.

This book was not written for surgeons but rather for occasional operators, or, more plainly, for medical men who should not operate at all. Whether there is a field for such effort or not the reviewer is unable to state.

J. R. McD.

Medical Service In Campaign. A Handbook For Medical Officers In The Field. By Maj. Paul Frederick Straub, Medical Corps (General Staff), U. S. Army. Leather. Pp. vii–169. Price $1.50 net. Philadelphia: P. Blakiston's Son & Co. 1910.

At the outbreak of the Spanish-American War few Army surgeons possessed practical experience under field service conditions aside from that gained in small campaigns against the Indians. This lack of experience was still more marked among the medical officers of the National Guard and among the other civilian physicians hastily called into the employ of the Medical Department. The sources of information as to his military duties available to the physician at that time were very limited. Since 1898 a great number of articles on medico-military subjects have appeared in the periodicals of this and other countries. The Manual for the Medical Department for our Army has been greatly enlarged, especially in the portion relating to the equipment and management of the sanitary units in time of war, and the Field Service Regulations, first published by our War Department in 1905, have carefully defined the status and duties of the sanitary personnel in active service. The latest addition to the literature of this subject is a volume entitled "Medical Service In Campaign" prepared by Maj. Paul F. Straub, Medical Corps, United States Army, under the direction of the Surgeon-General of the Army and published by authority of the War Department.

This book will prove of great value to all those connected with or interested in the military service. It contains little that is original with the author, but brings together in a small compass a large amount of useful information essential for the medical officer and which could otherwise be obtained only after a study of many books or from the teaching of considerable personal experience. The writer treats his subject in an up-to-date yet conservative manner and warns the reader that the lessons taught by our civil war are still of value in spite of improved weapons, and that "the procedures which demonstrated their practical value in earlier days should not be lightly thrown aside for new schemes evolved from the inner consciousness of theorists."

It was a common observation during the Spanish-American war that many physicians just recruited from civil life were entirely unable to grasp the importance of any of the functions of a medical officer other than those pertaining to his purely medical and surgical work. Major Straub, in writing of the degree of training necessary for the best interests of an army, says: "This state of efficiency can only be brought about by the requirement that, in addition to professional qualifications, medical officers shall be sufficiently instructed in such purely military subjects as may be necessary to enable them to act in harmony with the troops they are serving." To this end he introduces a chapter on field orders, their significance and interpretation, on map reading and on weapons in so far as they influence the character of wounds or effect the selection of suitable locations for hospitals and dressing stations. The text of these chapters is supplemented by numerous maps, diagrams, and tables.

The next chapter deals with the percentages of casualties, from both disease and wounds, which have attended campaigns in the past and which, as far as wounds are concerned, may be expected to be about the same in the course of future hostilities. The writer gives tables showing the numbers and proportions of each class of wounded which are to be anticipated and in the succeeding chapter on "Transportation" deals with the removal of those who are unable to proceed unaided to the rear. Attention is drawn to the fact that the long range of modern military rifles has greatly extended the danger zone during battles and therefore increased the difficulties and risks of promptly aiding and removing the wounded.

In the chapter on "Organization" reference is made to the recent increase from three to four in the number of medical officers attached to a regiment. The details of the care of the wounded from the firing line to the general hospital are fully covered in chapters entitled "Regimental Service and Aid Stations," "Dressing Stations," "Field Hospitals," "Stations for Slightly Wounded," and "Lines of Communication."

In the chapter headed "Administration," as well as elsewhere throughout the book, the importance of the administrative function of the Medical Department is emphasized, the ultimate object of which is "to bring the patient, the facilities for his treatment, and the surgeon in conjunction under the most favorable possible circumstances."

The writer frequently refers throughout the book to the important fact that "the basis of the organization of the medical department for war is the necessity of maintaining the highest possible effective strength of an army and of relieving it of its encumbrance of sick and wounded." It follows therefore "that a medical service in war is not organized and maintained with the sole object of meeting the humane demands of the age." The prompt evacuation of the wounded from the scene of active hostilities toward the rear is a cardinal point in effective administration, even though this removal may not always be for the best interests of certain individuals among the injured. The author clearly brings out the point that in the interests of military efficiency the care and treatment of the less severe cases of injury, which in large measure may recover soon and return to the front, is of more importance to the army than the care of the very serious cases which are not likely to render further service. This is a view too little appreciated and which it is hard for the civilian practitioner to grasp, because his greatest interest is in the severe and unusual injuries. The slighter cases of injury should not be sent to general hospitals far in the rear, but should be "treated as near as possible to the zone of operations, so that no unnecessary time will be lost in returning them to their organizations upon recovery. It is all important that some relation should be maintained between the distance that patients are to be transported and the probable duration of their disabilities."

The book is small in size, is conveniently bound in flexible covers, is printed on strong, well-glazed paper and is remarkably free from typographical errors. It should be part of the equipment of every medical officer in the National Guard. W. P. C.

THE PHILIPPINE
JOURNAL OF SCIENCE
B. MEDICAL SCIENCES

VOL. V DECEMBER, 1910 No. 6

AN EXPERIMENT WITH ORANGE-RED UNDERWEAR.[1]

By JAMES M. PHALEN.[2]

In his annual report for the fiscal year ending June 30, 1907, Lieutenant-Colonel William T. Wood, inspector-general of the Philippines Division, called attention to the experience of British army officers in India in the use of colored linings for their headgear, as well as to other experiments along the same line, and reviewed the recent literature bearing upon the subject. He recommended that an extended experiment be instituted in these Islands and that sufficient underclothing and hat linings of an orange-red color to equip several regiments be sent over here. This recommendation, upon being referred to the Surgeon-General and the Quartermaster-General, was concurred in and the latter recommended that 5,000 suits of orange-red underclothing and a like number of hat linings be authorized for the purpose. This was approved by the War Department, the clothing was prepared at the Philadelphia depot and shipped here, arriving in November, 1908. White underclothing of similar material was sent at the same time in sufficient quantity to equip an equal number of men, to be used as controls for the experiment. Upon the recommendation of the chief surgeon of the division, the details of the experiment were intrusted to the Board for the Study of Tropical Diseases, the members of which at this time were Captains James M. Phalen and H. J. Nichols, Medical Corps.

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[1] Read at the first biennial meeting of the Far Eastern Association of Tropical Medicine, held at Baguio, P. I., March 14, 1910.

[2] Captain, Medical Corps, United States Army, member of the United States Army Board for the Study of Tropical Diseases as they exist in the Philippine Islands.

THE SCOPE OF THE TEST.

In an indorsement from the office of the Surgeon-General, a number of suggestions for the carrying out of the experiment were made, the most important being as follows:

> In order that other conditions may be the same, the orange-red clothing should be issued to half companies occupying the same barracks; the special clothing should be worn at all times for at least a year, and the controls should have exactly the same clothing, except for color.
>
> If practicable, the same medical officers should remain on duty with the troops under observation for the entire period and should keep a careful record of the comparative amounts and nature of sickness among them; also of the subjective sensations of the soldiers as to comfort or discomfort in the sun, their mental and bodily vigor, etc.
>
> A number of officers and enlisted men who are specially susceptible to the effects of the sun should be equipped with the orange-red garments and required to report the results.

With these suggestions as a basis, the Board, in coöperation with Colonel J. van R. Hoff, the chief surgeon, drew up a plan for the experiment which was approved by the division commander. The main details for the test were as follows:

(*a*) The equipment of approximately 1,000 men with the colored underclothing and hat linings, with 1,000 men as controls to be furnished with white underclothing of similar texture. The men to be taken from different branches of the service and at widely separated posts so that all sections of the Islands should be covered. For this purpose the following troops, on account of the above reasons and because they had the necessary year to serve in the division, were selected:

Fifth Field Artillery, Fort McKinley, Luzon.
First Cavalry, Camp Stotsenburg, Luzon.
Fourth Infantry, Camp Jossman, Iloilo.
Twenty-third Infantry, Zamboanga, Mindanao.

(*b*) That the men who wear the special clothing and the controls should be taken from the same companies, which were to be equally divided in such a manner as to make the two groups as nearly similar as possible in physique; all men of long tropical service and those of exceptionally weak constitution to be excluded from the companies before dividing.

(*c*) That all officers, and especially those particularly susceptible to the effects of the tropical sun, should be invited to equip themselves with the special underclothing and report upon it at the end of the period of experiment.

(*d*) That a medical officer be detailed at each of the posts mentioned above, whose duty it would be to supervise the details of the test at his post. That these medical officers should not be separated from the troops equipped with the special clothing nor given duties that would interfere with the performance of this work. The medical officers selected for the duty were as follows: Fort William McKinley, Major C. C. Collins; Camp Stotsenburg, First Lieutenant G. L. McKinley; Camp Jossman, Captain L. M. Hathaway;[a] Zamboanga, First Lieutenant C. D. Cowles, jr.

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[a] Almost at the beginning Captain Hathaway asked to be relieved from this duty and First Lieutenant Hiram A. Phillips was detailed in his stead.

(*e*) That records be kept of the medical history of the men during the test, including the number of days lost by sickness and the nature of the illness.

(*f*) That the weight, strength test, and blood pressure be recorded at quarterly intervals for all the men.

(*g*) Blood examinations, including red and white counts, differential counts, and hæmoglobin estimations, to be made upon a limited number of men three times during the year.

(*h*) Observations to be made and recorded upon the pulse, temperature and respiration after exercise at frequent intervals.

(*i*) Special observation to be made as frequently as possible upon both sets of men after exercise, with a view to noting any symptom referable to climatic effects.

(*j*) A statement to be obtained from each wearer of the special underwear as to the individual advantages or disadvantages of the garments.

(*k*) The experiment to occupy the calendar year 1909.

THE GARMENTS.

The underwear and the hat linings designated for the experiment arrived in Manila about the first of December, 1908, and were distributed to the posts shortly thereafter. Difficulties began to be encountered upon the arrival of the requisitions. An undue proportion of small sizes of the garments was found to be present, this being particularly true of the orange-red undershirts. Only about 1,100 of the 5,000 sent were of sizes 36 and 38, which are worn by a majority of men. Therefore, rather more of a selection of men was necessary than at first was contemplated or thought desirable, a larger proportion of smaller men being required for the experiment.

The estimate of the War Department officials for five suits of underwear per man for the year, brought forth protests from a number of post and organization commanders, the calculations of the latter running from about eight to fifteen suits per man. As the purpose of the experiment would be defeated if an insufficient supply of the garments were furnished, it was decided that the needs of the wearers must be met. For the above reasons, the number of men actually equipped and kept under observation fell short of the original estimates. About 500 men in all were equipped with special underwear, including 20 men of the Hospital Corps at the Division Hospital, Manila, and 40 general prisoners at the Fort William McKinley prison. An equal number of controls with white underwear were used.

The undershirts issued were those that have been provided for some years past under the name of "*undershirts, cotton,*" a garment with a round neck, without buttons, and weighing approximately 8.5 ounces. The drawers were different from anything that recently has been issued, being a rather superior garment of heavy jean with webbing inserts at the seams. The weight of this garment was 8.9 ounces.

The colored garments when received were of a deep, orange-red color, the red predominating. The dyeing of the garments was very nearly uniform throughout the lot. Garments were washed and dried under varying conditions to test the stability of the dye. The first washing gave a distinctly red color to the water; however, this apparently was due to an excess of the dye, as the garments were not materially changed in color. Subsequent washings gave very little coloration to the water. The jean drawers lost their color faster than the softer undershirt. When the clothing was dried in the shade very little fading took place, but when exposed while wet to the sunlight the loss of color was very rapid. Here, too, the jean drawers lost color more rapidly than the undershirts. At the beginning of the experiment, garments were submitted to a local dyer for test, and he reported that they met the requirements of the soap and soda tests as recognized by the trade. The hat linings were not of a fast color; the first washing removed the greater part of the dye. As the washing of these articles was not contemplated, this was no great objection, except that rain and perspiration caused the color to run.

In actual use this clothing lost some color in a very short time. After a few months the garments presented all shades, from that approximating the original to a dirty cream-color. The same garment usually gave a variety of tints in proportion to the relative exposure to the sun. The red coloring matter was less resistant than the yellow, the first change being a rapid one from orange-red to yellow and then gradually to cream-color. The garments retained their color much better upon the inner than on the outer surface, showing the influence of direct sunlight upon the dye, and the much greater importance of this factor than that of the washing.

As the weight of these garments has been a matter of criticism, it will be of interest to note that by weighing a large number of the undershirts, both colored and white, it was found that there was an average increase of but one-fifth of an ounce due to the dyeing. As the colored drawers and those issued to the control were of different types, a like comparison was not possible, but the colored drawers averaged 1.2 ounces heavier than the white.

SUMMARY OF OBSERVATIONS.

The experiment, in accordance with instructions, was continued throughout the year 1909, the records being kept upon a blank furnished by the Board for Study of Tropical Diseases. By the end of the year the records, including those from outside sources, were completed. The several items contained upon the cards will be taken up serially and any discrepancies between the two groups pointed out as they come up, but the discussion of their significance will be withheld until the summary.

Weight.—The tables here given show comparative weights at three periods of the experiment—in January, in July, and at the end of the year, in December. The first table gives the weights of one hundred men of each group, selected because they arrived in the Philippines very shortly before the beginning of the experiment; therefore this table gives an indication of the change in weight of newcomers. In the second table are given the weights of all the men under observation.

TABLE I.—*Comparative weights of recent arrivals in pounds avoirdupois.*

Group.	Beginning.	Mid-year.	Loss.	End.	Loss.
Orange-red	139.3	135.0	4.3	136.2	3.1
White	140.9	137.7	3.2	137.6	3.3

Of the first group, 86 men lost weight, 11 gained, and 3 remained stationary. Of the second group, 79 men lost weight, 14 gained, and 7 remained the same.

TABLE II.—*Comparative weights of all men observed, in pounds avoirdupois.*

Group.	Beginning.	Mid-year.	Loss.	End.	Loss.
Orange-red	141.6	137.6	4.0	138.8	2.4
White	143.0	139.9	3.1	140.6	2.4

The difference between these two tables is very little, showing mainly a slightly greater average loss in weight for the new arrivals. The differences are greater in reality than appear in the tables. Whereas, the new arrivals almost uniformly lost weight in very nearly equal proportion, the older residents showed much greater variations, the losses and gains being more decided in character and more irregular. As a group, the inmates at the military prison at Fort McKinley gained an average of 1.3 pounds per man, although they fell off 0.8 pound in the middle of the year. A common feature of both tables and of both groups is the loss of weight, greater at the middle of the year than at its close. The obvious explanation of this phenomenon is the higher average temperature during this time of the year and the consequent greater loss from perspiration. Comparing the two groups, it is of interest to note that the loss of weight of those wearing the special clothing was materially greater at the mid-year period than that of the group wearing white. This difference does not appear at the close of the year.

Blood counts.—The blood of 123 men was examined at the beginning of the year, but because some of the men left the division, the last of the three examinations included but 115 men. The red and white corpuscle counts were made with a Thoma-Zeiss hæmocytometer and the hæmoglobin estimates with the Dare instrument. In the differential count no attempt was made to divide the lymphocytes into groups and the differentiation between this class and the large mononuclears was made upon their staining reactions rather than upon their sizes.

TABLE III.—*Blood examinations.*

Period and group.	Erythrocytes.	Hæmoglobin.	Hæmoglobin index.	Leucocytes.	Polymorphonuclears.	Lymphocytes.	Large mononuclears.	Eosinophiles.	Mast cells.
At beginning:		*P. ct.*	*P. ct.*		*P. ct.*	*P. ct.*	*P. ct.*	*P. ct.*	*P. ct.*
Orange-red (66 men)	5,085,100	93.5	91.9	7,122	55.2	35.6	5.3	3.2	0.7
White (57 men)	5,075,000	89.6	88.3	7,475	57.8	33.3	5.3	2.7	0.9
At mid-year:									
Orange-red (62 men)	5,156,000	91.6	88.8	7,552	58.3	32.2	6.1	2.8	0.6
White (56 men)	5,090,000	88.4	86.7	7,305	59.4	32.9	4.0	3.4	0.3
At end:									
Orange-red (61 men)	5,346,000	92.4	86.4	6,868	55.4	36.3	5.0	2.5	0.8
White (54 men)	5,184,000	89.2	86.0	7,372	58.7	32.6	4.6	3.6	0.5

The results of these examinations agree in character if not in degree with those made by Captain W. A. Wickline, Medical Corps, whose excellent work along this line at Camp McGrath in 1905–1906 appeared in one of the late volumes of the Military Surgeon. In both groups, as in Captain Wickline's subjects, there was an increase in the number of the red cells and a decrease in the percentage of hæmoglobin, the hæmoglobin index showing necessarily an even greater diminution. The differential leucocyte count shows the same high proportion of lymphocyte cells, this increase being at the expense of the polymorphonuclear cells. This variation from the normal proportions appears in the first count and is quite uniform throughout the three examinations. The disparity between these counts and those of Captain Wickline, whose earlier examination showed a fairly normal proportion in the white cells, is due to the fact that Captain Wickline's subjects were largely new arrivals from the United States, while the examinations here reported were mainly on men who had served for a year or more in the Philippines.

The chief difference noted in the two groups is the greater increase in the red cells with a greater decline of the hæmoglobin index in the group wearing the special underclothing. One explanation of the erythrocyte increase in the Tropics is that it is due to excessive perspiration, which, by concentrating the blood, gives an increase which is not actual but only relative to the fluid elements. The other theory is that the increase is an actual one, the number of red cells being augmented by the stimula of heat and light upon the blood regenerating organs. Whatever weight of evidence may be attached to our examinations, the results are strongly in favor of the first explanation. As will be shown later, the heat is greater under the orange-red underwear and perspiration more profuse, while the actinic rays of the sun, which are credited with causing the increased stimulation according to the second theory, are retarded by the color.

Blood pressure.—The instrument used in these investigations was the Riva-Rocci, as modified by Doctor Cook of New York, this instrument having a 4-inch arm piece. Only the systolic pressure could be measured with this apparatus, but as comparative results alone were needed, this was not a serious objection.

The following table gives the average readings of the two groups at quarterly intervals. About 2,000 observations were made upon 480 men wearing the special underwear and about 1.500 observations upon 420 men wearing the white. The readings are in millimeters of a mercurial column.

TABLE IV.

Group.	January.	April.	August.	December.
	mm.	*mm.*	*mm.*	*mm.*
Orange-red	124.8	121.1	117.9	125.5
White	123.3	120.6	118.1	122.9

It will be seen that there was a noticeable falling off in blood pressure in April, 3.7 millimeters for the special groups and 2.7 for the controls. This is explainable by the great increase in atmospheric temperature from January to April and the consequent loss of body fluids by perspiration. In August there is a still greater drop in pressures, the loss from the first of the year being 6.9 millimeters for the special group and 5.2 millimeters for the white group. The heat of April, although modified by rains, has moderated but little, while the long continued heat, together with increased humidity has had its enervating effects. However, by December, the climatic conditions of January are closely approximated and it is seen that the average blood pressures have increased to very nearly or quite their original point. At the end of the year the average of the special group was 0.7 millimeter over that of January, while for the white group there was a loss of 0.4 millimeter. A comparison of the two groups shows that during the hot periods the loss for those wearing the orange-red was slightly greater than for those wearing white, a logical effect of the increased perspiration for the first group.

Temperature, pulse and respiration.—These observations were taken as soon as possible after the subjects had completed a tour of drill or fatigue duty or other exercise causing exposure to the sun's rays. A total of about 4,000 observations were taken upon each set of men. The following table gives the average of 1,500 observations upon each group. Only the figures are given at this time, any abnormalities of the rhythm or quality of the pulse or respiration being noted under another heading.

TABLE V.

Group.	Temperature.	Pulse.	Respiration.
	°*F.*		
Orange-red	98.792	91.2	22.2
White	98.780	90.9	21.3

The variation from the normal temperature is very slight in either group, and the difference between the two is so slight as to be wholly negligible. In both, the pulse and respiration rates are higher than the normal, and in both instances the special group of men show higher rates than the controls, although these differences are not very marked.

Strength tests.—At the outset of the experiment a requisition was made for hand dynamometers of a certain make, the object being to keep a record of the strength of the subjects of the test. The instrument asked for was one that not only marked the force of the grip but also the time for which it could be sustained. The apparatus sent did not meet the requirements, as it registered only the strength of the initial grip. A large number of observations were made with this instrument but they were found to be of no value whatever without the element of time. It was observed that a man greatly fatigued, whose strength as recorded by the more elaborate ergometer was depressed 50 per cent from the normal, could still muster strength for the moment practically to equal his normal grip. For these reasons no tabulation of the strength is given. The Brem's ergometer was used only for special experiments, it being too large and heavy to be of general use in the test.

Comparative sick reports.—The table which follows gives a comparison of the number of cases of illness of the different classes together with the number of days lost from each cause, and for better comparison the cases and days reduced to rates per thousand men. All cases of injury or other accidental disease, venereal diseases and other causes of admission upon which climate could have no effect have been excluded from this comparison.

TABLE VI.

Cause.	Orange-red group (450 men).				White group (420 men).			
	Admissions.		Days lost.		Admissions.		Days lost.	
	Number.	Rates per 1,000.	Number.	Rates per 1,000.	Number.	Rates per 1,000.	Number.	Rates per 1,000.
Heat exhaustion	12	27	53	117	9	21	27	64
Malaria	69	153	433	962	64	152	493	1,174
Febricula	17	37	95	211	20	48	109	259
Dengue	25	55	195	433	17	40	155	369
Climatic bubo	6	13	183	406	5	12	140	333
Rheumatism, muscular	8	17	102	226	7	16	35	83
Gastro-intestinal	45	100	259	557	36	85	238	566
Respiratory	16	37	115	255	19	45	126	300
Nervous	3	7	14	31	6	14	31	74
Skin	28	62	148	328	19	45	126	300
Total	229	508	1,597	3,526	202	478	1,480	3,522

While there are considerable variations for certain causes of admission, these about balance each other, and the rates per 1,000 for admissions and days lost very closely approximate each other. The slightly higher rate for heat exhaustion in the special group is worthy of note, although there is little else in this table that is significant.

Symptoms referable to climate.—There are a number of symptoms which are well recognized as being due to the effects of heat and sunshine, and these as observed after the men have been at drill or fatigue duty or upon practice marches, are given in the next table. It is practically impossible to reduce these two groups to a common basis, but the numbers of observations upon them approximately are equal.

TABLE VII.—*Symptoms due to the effects of heat and sunshine.*

Manifestations.	Orange-red group.	White group.	Manifestations.	Orange-red group.	White group.
Headache	179	146	Faintness	7	5
Dizziness	53	64	Muscular weakness	7	15
Feverish sensation	31	28	Muscular pain	6	7
Excessive thirst	7	9	Pain in eyes	5	1
Dryness of lips, mouth and throat	9	13	Precordial pain	2	3
			Sore throat	7	6
Blurred vision	33	23	Coryza	8	20
Nausea	21	26	Chilly sensations	5	4
Vomiting	3	3	Nervousness	2	3
Pulse, irregular	7	4	Dyspnœa	0	3
Pulse, intermittent	10	12	Tachycardia	2	2
Pulse, weak	39	32	Tinnitus aurium	1	0
Excessive perspiration	21	2	Fell out on drill or march	10	10

This table shows that the two groups of men suffered in very nearly equal proportions from the effects of the heat, the greatest variations being in the item of excessive perspiration, in which the special group gave a much greater proportion than the controls. As this phenomenon was the evidence of the medical officers and not the statement of the subjects observed, it is a significant fact. The other symptoms vary to an extent that could be accounted for by the laws of chance, and therefore are of no special signification.

Impressions of the wearer.—At the close of the experiment each man who wore the orange-red underwear was asked to give his opinion of it, and to express his views as to its advantage or disadvantages.

The tendency of the man was to give the consensus of opinion of the organization as his own, but this was overcome as far as possible by a list of questions previously prepared. Of the whole number only 16 men preferred the colored underwear to white; that it was cooler, was the reason assigned by 7 men, while 4 declared that it relieved them of headache and dizziness; relief from headache, fever, and prickly heat each were assigned by one man as a reason for preferring the colored garments, while the remaining 2 men paid the clothing the doubtful compliment that it did not show the dirt like the white; 54 men stated that they experienced no effect one way or another from the clothing and that they had no choice between the colors. A decision adverse to the colored underwear was pronounced by all the rest of its wearers, nearly 400 in all. In 50 instances it was declared to be hotter than the white, while 104 men expressed the same idea by saying that it caused more profuse perspiration. It was perhaps the same impression that caused 21 men to declare it too heavy; 64 said that it felt more "uncomfortable" than the white, many attributing this to the irritating effect on the skin. Other complaints relative to the skin were that it "scratched," given by 5 men; that it "caused itch," given by 3; that it "caused skin disease," given by 2; while 6 complained of its causing prickly heat. Two of the latter said they had never suffered from this complaint until wearing this underwear and that it had since been persistent. The appearance of the underwear was apparently distasteful to a number of men, especially after the garments had faded. Fifty-two men objected to the clothing because of its fading, while 42 disliked its appearance after washing, declaring it "dirty looking," "lacking in neatness," and "unsanitary." The staining of the outer clothing from the dye was mentioned by 2 men. Four spoke of a bad odor from the clothing and this was mentioned by one of the organization commanders. Among the effects charged to the clothing, by lesser numbers, were headache, dizziness, fever, blurred vision, boils, colic, and a tendency to catch colds.

It is not to be doubted that there was some prejudice against the clothing in the minds of the wearers. This was due to the fact that they were rendered conspicuous and were subjected to bantering by their companions. The fact that they were charged with experimental clothing also had a bad effect. Despite this handicap it is thought that the criticisms of the clothing by the men were made in all sincerity, and expressed their true impressions of the test.

All the organization commanders who reported upon the clothing, expressed the opinion that no effect was apparent from its use. The lack of stability of the dye was commented upon by all and the general opinion was that the colored clothing was heavier and caused more perspiration than the white.

The special underwear was given a trial by sixteen officers. In a majority of cases it was discarded after a short time because its weight was greater than that usually worn and it was therefore much hotter. This objection induced the members of this Board to have the nainsook underwear, as sold by the quartermaster department, dyed by a local dyer to the same color as the special clothing. This was an improvement, but the writer could see no advantage in the colored clothing over the white of a similar weight. Only one unqualified expression of approval came from these officers, and this was from one who stated that he always had experienced a feeling of depression of spirits and irritation after exposure to the sun previous to wearing the colored underwear, but that this had been relieved entirely by its use. He was convinced that it was the proper clothing for use in the sun, but added that it kept him slightly warmer than did the white.

EXPERIMENTAL EVIDENCE.

It can be accepted without question that a fabric of red or orange-red color is highly protective against those chemical rays of the sun which reduce the photographic plate. Other colors have varying degrees of protective influence, but all are protective to some extent. However, the protection afforded by a fabric depends not only on its color, but upon its thickness and the tightness of its weave. A great deal of information has been obtained by exposing to sunlight photographic plates covered by fabrics from the different articles of the uniform. By adding to these fabrics layers of the colored and white underwear and the orange-red hat linings, a good idea was obtained as to the increased protection from the actinic rays of the sun afforded by the colored garments. The most interesting result is that the campaign hat, two varieties of which were used, is as opaque to chemical rays without a red lining as with it. The lining materially added to the opacity of the khaki cap, and showed a slight improvement over the ordinary lining of a green or brown color as seen in the caps bought of the military supply houses.

A comparison of the English and American khaki shows that the added weight and tighter weave of the latter increased the degree of protection afforded against the rays which reduce the photographic plate when the exposure was as short as could be made with the slide shutter. A longer exposure of the English khaki with the colored and white undershirt shows what a material difference in opacity the orange-red color produces. The same kind of experiments were made, using material from the blue flannel shirt, the olive-drab shirt, and the blue chambray shirt in the same manner. Not much would be expected from the chambray shirt, but the blue and olive-drab flannel shirts were shown to be not nearly so protective chemically as would be expected.

It is a widely, but not universally accepted theory that the pigment in the skin of the dark-hued races is an effect of the chemical rays of the sun, and that its purpose is to protect the organism from the deleterious influence of these rays. Certain it is that sunlight increases the deposition of pigment in the skin as it shown by tanning in the white race. That the dark pigment of the Malay or the Negro is due to a like cause is not so apparent and that it was deposited for the purpose of protection from the sun is rather difficult of proof. If a determination of the chemical nature of the skin pigments of the different colored races has ever been made I am unaware of it. Sambon, of London, photographed the spectrum of an electric arc lamp after passing the rays through the skin of a native of India and then constructed a cloth that would have the same effect. This cloth was of a dark color externally, and red inside.

To determine the relative opacity of the skin of different degrees of pigmentation, specimens were obtained from an exceptionally white subject, from a light Filipino, and from one of the darkest subjects obtainable. These specimens were subjected to the same photographic tests as the fabrics mentioned above. The skin specimens were first prepared by removing all subcutaneous tissue and making them as nearly as possible of uniform thickness. By reference to a series of photographs, comparing the very dark skin with the white, it could be seen that the former, as expected, was more resistant to light than the latter. The difference was most noticeable for the shorter exposures, being much less so as the time of exposure is increased. It could be seen that the white skin was quite opaque to the chemical rays, and that when the time of exposure was increased to one minute the effects on the photographic plates did not differ very greatly. The effect upon the plate produced by a one-minute exposure through the dark skin was approximated in about one-fourth that time through the white. A comparison of the effect produced through the light brown and the white skins gave almost no difference in their degrees of opacity during a fifteen-second exposure, and those of less duration produced no greater variation. The added effect of the texture of the skin was shown. Both the white and the dark brown were firm and tough, while the light brown was of a much softer texture. It is apparent that the superior density of the white skin has compensated for the increased pigment of the light Malay. Another photograph was made giving a fifteen-second exposure through the darkest skin and through the white skin reinforced by one layer of khaki uniform cloth. It was observed that the khaki material completely neutralized the difference in opacity which exists between the two.

A comparison of these photographs with those made through the fabrics showed another important fact. It will readily be seen that the pigment of the darkest skin does not by any means approximate the orange-red of the experimental garments in the matter of excluding the chemical rays, and this is the more remarkable when the thickness and close texture of the skin is contrasted with the lesser thickness and loose weave of the undershirt used. This observation is in support of the statement of Doctor Freer, of the Philippine Bureau of Science, that the obstruction offered to the chemical ray by red or similar color is not due to any inherent quality of the color as such, but varies with the chemical nature of the dyes used.

One of the earliest and most persistent complaints against the orange-red underwear was that it was hotter and caused more perspiration than the white. If this could be proved and the difference in temperature found to be at all great, the fact would be a serious objection to its further use. In order to determine how much foundation there was for these complaints the following experiments were carried out:

Experiment No. I.—Two thermometers were first tested by heat and cold to see that they registered equally.

Experiment No. II.—The thermometers were placed, one behind a screen of orange-red and the other behind a screen of white, both screens being made of the undershirt material. After an exposure of the screens to twenty minutes of direct sunlight, with free circulation of air around the thermometers, both registered 36° C.

Experiment No. III.—The thermometers were inclosed in equal thickness of the two materials. After twenty minutes the one inclosed in orange-red registered 52° C., while that inclosed in white registered 44.6° C. The thermometer inclosed in white attained its maximum more quickly than that in the red.

Experiments Nos. IV and V.—Thermometers were placed in empty flasks and covered with orange-red and white undershirt material, and in flasks of ice water covered in the same manner and exposed to sunlight. The table below shows the variations in the temperatures, in degrees centigrade.

TABLE VIII.

Exposure.	Air temperature.		Water temperature.	
	White.	Orange-red.	White.	Orange-red.
	°*C.*	°*C.*	°*C.*	°*C.*
Beginning			8.0	8.0
After 10 minutes	39.0	41.0	11.0	10.5
After 20 minutes	41.2	43.5	13.8	14.2
After 30 minutes	43.0	46.0	16.2	17.5
After 40 minutes	43.2	47.0	19.0	20.5
After 50 minutes	43.5	48.0	21.5	23.4
After 1 hour	44.0	48.2	23.2	25.2
After 1½ hours			27.0	29.6

The irregular changes in the temperature are accounted for by the presence of fleecy clouds which at times mitigated the effect of the sunlight.

Experiment No. VI.—The last experiment was repeated, except that hot water was used and the flasks allowed to remain in the shade.

TABLE IX.

Exposure.	Water temperature.	
	White.	Orange-red.
	°C.	°C.
Beginning	75.0	75.0
After 10 minutes	71.0	72.0
After 20 minutes	68.5	70.0
After 30 minutes	65.2	67.0
After 40 minutes	63.0	65.0
After 50 minutes	59.0	61.0
After 1 hour	57.5	59.5

Experiment No. VII.—A composite shirt was made by sewing together one-half of an orange-red garment and one-half of a white one. This was put on a man and clinical thermometers, protected with corks to keep them away from the surface of the body and the cloth, were suspended, one under each side. After ten minutes' exposure to the sun the thermometer beneath the white side registered 37°.75, while that beneath the orange-red registered 43°C.

The thermometers were then permitted to lie against the body, with the shirt in contact with the instrument. Ten minutes' exposure resulted in a record of 36° under the white and 37°.25 under the orange-red. During the experiment the subject perspired profusely. He reported the perspiration first on that side covered by the orange-red, and the moisture appeared through the cloth very much earlier on this side than on the white.

The experiments with the air and cold water temperatures were repeated except that in each case the materials used were covered with a layer of khaki cloth. The same results were obtained, differing only in degree, there being not so much difference between the temperatures as when nothing intervened between the sun's rays and the undershirt material.

UPON THE PHYSIOLOGICAL EFFECTS OF MOIST HEAT.

Through the kindness of Captain P. L. Boyer, Medical Corps, we were enabled to make use of the bathrooms at the hospital at Los Baños for a series of experiments, the purpose of which was to show what effects would be produced upon the human organism by exposure to a high degree of heat and moisture. The subjects were volunteers from the detachment of the Hospital Corps, stationed at the hospital. For the purpose of the experiment one of the bathrooms was placed at our disposal. This consisted of a room about 15 feet long by 8 feet wide into which, at one end, opened a small steam room, this latter being situated immediately above one of the hot springs. The temperature could be raised by allowing hot water to run in the bathtub in the large room, or by opening the door of the steam room to the necessary degree, and by the same means the moisture in the atmosphere could quickly be raised to the saturation point. The room was provided with a small window at one side and a door at the end, both fitted with slats, allowing quite a free draft across a section of the room and keeping the whole place well ventilated.

Four subjects, in good physical condition, were selected and these were subjected, two at a time, to four hours in a temperature of from 92° to 98° F. as recorded by a wet-bulb thermometer. The atmosphere was kept saturated with moisture as evidenced by the dripping of water from the walls and by records of wet and dry bulb thermometers. The subjects, clothed in suits of thin nainsock underwear and socks, entered the bathroom where settees of rattan, upon which they could recline, were provided. The experiments in each case were begun in the early afternoon, soon after the noon meal.

SUBJECT No. 1.—*J. F., age 24 and weighing 146.5 pounds.*

Exposure.	Room temperature.	Pulse.	Respiration.	Temperature.	Blood pressure.
	°F.			*°F.*	*mm.*
Beginning	92	80	18	98.8	135
After 30 minutes	92	80	18	99.2	
After 1 hour	93	78	22	99.8	
After 1½ hours	94	80	22	100.0	
After 2 hours	94	84	22	100.0	
After 2½ hours	95	84	24	100.2	
After 3 hours	95	92	24	100.4	
After 3½ hours	95	94	24	101.0	
After 4 hours	94	90	22	100.2	118

The subject lost 2.5 pounds in weight, and his strength as recorded by the Brem ergometer fell off 48 per cent during the experiment. However, he was able to record as strong a grip with a hand dynamometer after as before the experiment.

SUBJECT No. II.—*W. R., age 19 years and weighing 139 pounds, a short muscular subject.*

Exposure.	Room temperature.	Pulse.	Respiration.	Temperature.	Blood pressure.
	°F.			*°F.*	*mm.*
Beginning	92	72	18	98.6	128
After 30 minutes	92	80	20	99.6	------
1 hour	93	84	23	100.0	------
1½ hours	94	94	22	100.2	------
2 hours	94	88	22	100.2	------
2½ hours	95	90	23	100.4	------
3 hours	95	94	24	100.4	------
3½ hours	95	94	24	100.4	------
4 hours	94	90	22	100.2	102

The loss of weight in this subject was 3 pounds, and the ergometer showed a decrease of 58 per cent in strength.

SUBJECT No. III.—*F. F., age 25 years and weighing 136 pounds.*

Exposure.	Room temperature.	Pulse.	Respiration.	Temperature.	Blood pressure.
	°F.			*°F.*	*mm.*
Beginning	95	76	14	98.4	124
After 30 minutes	95	96	16	99.5	------
After 1 hour	96	96	18	99.6	------
After 1½ hours	96	92	18	99.8	------
After 2 hours	97	92	16	100.0	------
After 2½ hours	98	96	18	100.4	------
After 3 hours	98	96	20	100.4	------
After 3½ hours	98	104	22	100.6	------
After 4 hours	98	112	22	101.2	116

The loss in weight in this case was 4 pounds and the loss of strength, as shown by the ergometer, was 26 per cent.

SUBJECT No. IV.—*O. H., age 24 years and weighing 141 pounds.*

Exposure.	Room temperature.	Pulse.	Respiration.	Temperature.	Blood pressure.
	°F.			*°F.*	*mm.*
Beginning	95	74	18	98.6	135
After 30 minutes	95	80	20	99.0	------
After 1 hour	96	92	28	100.0	------
After 1½ hourrs	96	88	28	100.0	------
After 2 hours	97	88	26	100.2	------
After 2½ hours	98	88	25	100.4	------
After 3 hours	98	96	28	100.4	------
After 3½ hours	98	96	28	101.0	------
After 4 hours	98	96	28	101.4	120

This man lost 3.5 pounds in weight and 21 per cent in strength.

The writer remained with these men during the entire time of the experiment and made the observations. The men were told that if they cared to do so they could take a nap or smoke, or occupy themselves as they pleased. They all settled themselves for a restful afternoon, but in a very little time they became wakeful and restless. After sitting on the settees for a short time they began to walk around the room. They smoked and carried on fragmentary conversation, but the restlessness remained during the afternoon. Sweating was very profuse and the clothing soon was saturated. A noticeable change took place in the character of the respiration; inspiration became slow and deep with quick expiration and then an interval before the next inspiration. The pulse in each case retained its quality, the only change being in its rapidity. Each of the four men denied the presence of headache or other disagreeable symptoms, although the writer suffered from quite a severe headache. All felt tired and relaxed at the close of the experiment and without appetite for the evening meal. Drowsiness quickly supervened upon the restlessness after quitting the bathroom. No effects were experienced by the men the next day.

Observations of a somewhat similar character were made upon fifteen men of a baseball squad. The men were seen on three of the hottest days in August, the temperature according to Manila observatory reaching 93° F. each day and the relative humidity approximately 80 per cent. The sun temperature on the field could be made to register up to 130°, according to how much reflected heat reached the instrument. During the time, the sky was cloudless but there was a very moderate wind. The observations were taken after about two hours of hard baseball practice, from 1.30 to 3.30 in the afternoon. The men were perspiring freely and most of them were red of face from the exercise. The average of the temperatures taken under these conditions was 99°.7 F., the lowest being 99° and the highest 100°.4. The blood-pressure readings gave an average of 129.3 millimeters, the average at the beginning being 120.7 millimeters. It was not possible to get the pressures on all of the men after the effects of the exercise had worn off, but they were obtained in six cases, when the average was 121.5 millimeters, the same men giving an average of 129.5 millimeters after exercise.

THE CLIMATE.

The following short summary of climatic conditions in the Philippine Islands is introduced at this time so that the *important features may be fresh to the mind* in considering the final decision of the test. The climate varies somewhat throughout the Islands, but a consideration of the climate of Manila will answer for that of the entire lower elevation which comprises the great bulk of the inhabited parts of the Islands. To the newcomer who arrives in Manila, the climate seems to be ideal during the first part of the year. Although the middle of the day is hot, the hours of the early morning, and those of the evening after 5 o'clock, are cool and the nights are sufficiently cool to render the use of a light blanket necessary. During the month of January there are occasional showers, but the rainfall is light. However, the average number of hours of sunshine is much above the mean for the year, and the humidity is relatively high. This complex of atmospheric conditions produces a climate which is very pleasant when one is shaded from the sun. Nevertheless, even light exercise such as walking quickly brings on profuse perspiration and as the moisture does not evaporate rapidly on account of the high humidity, it causes considerable discomfort. Even at night, walking is very likely to be associated with disagreeable perspiration.

As the year advances there is a gradual change in the climate; the temperature, still moderate through February, rises rapidly through the two succeeding months and reaches its maximum in May. The rainfall reaches its lowest figure in February, rising gradually through March and April, and rapidly in May. With this increase in rainfall there is a corresponding rise in vapor tension, but this increase is not as rapid as that of temperature, so that while the actual amount of vapor in the air is increasing, the relative humidity falls steadily until April, when it bounds upward during the two following months. In number of hours of sunshine there is a steady rise to include the month of April, after which there is a sharp decline.

The months of April, May, and June comprise the season which without doubt is the most disagreeable of the year. The temperature reaches its maximum in May, however it is only slightly higher than in the other two months. The relative humidity, low in April, rises rapidly during the two following months. The rains, although they are more frequent, are not sufficient materially to affect the temperature, and in the early part of this season there is a great deal of sunshine. Another feature which adds to the discomfort of this season is that it is the time for the change in the monsoons from the northeast to the southwest, and there is no regular monsoon blowing. Such winds as do prevail are likely to be gusty and changeable and to help little toward modifying the temperature. In this season any exercise is accompanied by profuse sweating, and the shade of a room frequently is not sufficient to render conditions comfortable. Even at night, it is at times so hot and humid that there is great discomfort trying to sleep, because of excessive perspiration.

With the establishment of the southwest monsoons in June there is an increase in the rainfall, which, together with the winds, materially affect the climatic conditions. During the succeeding three months rains are of almost daily occurrence and typhoons are liable to occur. The temperature still maintains a high mean and the humidity is high. The sun is not visible as often as earlier in the year, but when it does shine its heat, combined with the moisture in the air, renders the climate very hot. Conditions as to personal comfort are much the same as during the preceding season except that the discomforts are of a less degree. The heat moderates in October, both vapor tension and relative humidity are less, and the rainfall decreases greatly. The changes continue, until by the first of December the conditions as described for January are again approximated.

The following table is a summary of the climatic conditions in Manila. These figures are prepared from the reports of Rev. José Algue, S. J., Director of the Philippine Weather Bureau, and in most instances are the averages for a number of years. The temperatures have been reduced to the Farenheit standard and the metric measurements to inches.

Month.	Temperature.			Humidity.		Precipitation (average monthly).	Wind.		Hours of sunshine (daily average).
	Mean.	Mean maximum.	Mean minimum.	Mean relative.	Absolute.[a]		Prevailing direction.	Velocity per hour (average).	
	°F.	*°F.*	*°F.*	*P.ct.*	*Gr.*	*Inches.*		*Miles.*	*h. m.*
January	77	85.6	69.3	77.6	7.7	1.14	N.	4.8	6 13
February	77.7	86.9	69.1	74.2	7.4	0.39	E.	5	7 20
March	80.2	89.8	71.4	71.8	7.8	0.73	E.	5.8	7 57
April	83	94.3	73.8	70.7	8.5	1.08	E.	6.1	8 51
May	83.5	92	75.5	76.7	9.2	4	SW.	6.6	7 38
June	82.2	89.8	75.4	81	9.7	9.75	SW.	6.4	5 30
July	80.8	86.3	75	84.8	9.7	15	SW.	6.8	5 0
August	80.8	86.9	74.9	84.8	9.7	14.2	SW.	7.6	4 37
September	80.6	86.9	75	85.5	9.7	14.7	SW.	8.1	5 5
October	80.4	87.8	74	82.7	9.2	7.55	SW.	5.6	5 35
November	79	86.3	72.5	82	8.7	5.37	N.	4.4	5 24
December	77.3	85.4	70.7	80.7	8.2	2.27	N.	4.2	5 16
Annual	80.2	88.2	73	79.4	8.7	76.31	-------	6	6 12

[a] The absolute humidity is expressed in grains of aqueous vapor per cubic foot of air.

The average person when discussing the climate of these Islands takes no middle ground: he either pronounces it ideal, thus ranging himself with a select minority, or else conveys the impression that there are no words in his vocabulary properly to express his disapproval of it. However, moderation in discussion is beginning to make its appearance and somewhere between these two opinions lies the truth. To the writer, the year appears to be divisible into two parts so far as personal comfort is concerned. That half of the year beginning with the first of October and ending with the last of March is a season when with little effort one can be comfortable, and three months in the middle of this season are almost faultless. On the other hand, the season from the first of

April to the last of September is one of great discomfort on account of heat, humidity and rainfall, and these discomforts are the greater in proportion to the amount of exposure to the weather. To those persons who are in the habit of saying that the heat of Manila is as nothing compared to that of certain parts of the United States throughout the summer, the following table will be of especial interest. The places in the United States are selected because they are the ones referred to as especially hot in summer and surely most of them would not be regarded as summer resorts. The following table gives the mean temperatures and humidity rates for these places for the month of July and the corresponding figures for Manila for the entire year.

TABLE X.

Locality.	Mean temperature.	Humidity.	
		Relative.	Absolute.
	°F.	*P. ct.*	*Gr.*
Chicago (July)	72.3	70.6	----
New York (July)	73.7	70.4	6.3
St. Louis (July)	78.8	67.9	6.8
Washington (July)	77.0	71.0	6.7
New Orleans (July)	81.7	72.3	8.0
Jacksonville (July)	82.5	71.8	8.6
Manila (annual)	80,2	79.1	8.7

It will be seen from this table that it is only in the Southern States that the weather conditions of summer approximate those of the Philippines for the entire year. It is only when the Gulf States are reached that the mean summer temperatures reach the annual mean for Manila, and even then the humidity remains much lower. It is in no spirit of carping criticism that these comparisons are made, but only to point out that no mysterious influence need be invoked to account for deterioration, while we have with us the high mean temperatures and humidity that obtain in these Islands.

However, in view of these figures, it is only just to say that it is surprising how little actual discomfort is experienced from the climate. The chief factor in rendering these Islands as comfortable as they are is their location in the track of the seasonal winds. What the climate would be without the influence of the monsoons can be imagined only during the period of calm, when the monsoons are changing in April. Another factor is that the resident here realizes at once that it is necessary to adapt his clothing, his work and diversions, in fact his whole habits of life to the local conditions of the climate. To one who is unable to do this, as for instance the soldier in field duty, the climate must remain one of unusual severity.

SUMMARY AND CONCLUSIONS.

Before pronouncing judgment upon the results of this experiment, it will be necessary to bring together and coördinate the evidence presented heretofore. It can be conceded at once that orange-red underclothing protects the body from the chemical rays of the sun, at least for those rays that act upon the photographic plates. As to the change in color due to fading, this was extreme only where the clothing was exposed to direct sunlight and on the whole was not so great as to interfere with the success of the test. This fading undoubtedly created a prejudice against the underwear, as after a few washings its bizarre coloring could not fail to outrage the sensibilities of the wearer.

In comparing the results of the various tests made, the following evidence is adduced:

(*a*) There is a loss of weight in both groups, greater by nearly a pound per man in the hot season for the special group.

(*b*) Blood examinations show the two changes due to tropical climate—increase of red cells and loss of hæmoglobin—more pronounced in the special group than in the white.

(*c*) Blood pressure shows a fall in both groups during the hot and rainy seasons with a return to about normal in the cool of December. The loss is greater during the middle of the year for the special group than for the white.

(*d*) Temperature, pulse and respiration all show a slightly higher rate for the special group than for the white. The differences are so slight that taken singly they would have no significance, but together with the rest of the tests, they are suggestive of more than accident.

(*e*) The evidence adduced from the comparative sick reports is negligible except that admissions from heat exhaustion and febricula, most of the latter probably due to heat, were not reduced by wearing the special underwear.

(*f*) Symptoms due to heat about balance in the two groups, so that there was apparently no benefit derived by the special group.

(*g*) After giving due weight to the prejudice against the clothing, the persistent complaints of greater heat, greater weight and increased perspiration lead to the conclusion that the colored garments are more receptive to heat rays than are the white. The experiments recorded above support this view.

The physiological effects of the climate here shown in loss of weight, lowered blood pressure and increase in temperature, pulse and respiration, have been reproduced experimentally in an exaggerated degree by the influence of moist heat without the aid of the sun's rays. That these effects can so constantly be produced can not be questioned. On the other hand, there is no evidence that these effects can be brought about by the sun's rays alone, and ordinary experience teaches us that they are not so produced. It is a strongly suggestive fact that the stress of the climate, as evidenced by loss of weight, depressed blood pressure, increased temperature, pulse, and respiration, with heat strokes and febricula, is felt by the system during the hot and moist days of May to October rather than during the bright days of January to May. The rôle that humidity plays as an adjunct to heat is that of an interference with heat loss by evaporation. As evaporation from the skin is the main process by which a balance is maintained between heat production and heat loss, such an interference is serious. With a high external temperature and heat loss practically abolished by humidity, we have, as Sutton says, a vicious circle established. With the rise of internal temperature, oxidation in the system is increased with production of more heat and a still greater rise in body temperature. The progressive action of these factors on temperature, pulse and respiration are well illustrated in the experiments with moist heat described heretofore.

The photographic work with skins of varying pigmentation suggests that such pigment is of no great protection from actinic rays. It is probable that the effects of the chemical ray are exhausted upon the skin alone. Even in the deeper layers of the skin there is a constantly circulating layer of blood which is probably much more efficient as a protection against the chemical ray than is the permanent layer of pigment. If the effect upon the skin can be accepted as a measure of actinic influence, then the khaki is of itself sufficiently protective. Many men have their arms protected only by one layer of khaki material and after years of service in the Tropics have no more pigment in the skin thereof than they had upon arrival.

A final judgment then is that the test underclothing has added materially to the burden of heat upon the system, a burden which undoubtedly is the great cause of tropical deterioration. To balance this, it is protective against the chemical ray, the influence of which is regarded as of little moment, and which is sufficiently excluded by khaki clothing and the campaign hat worn at present. Certainly no beneficial effect whatever was observed from the use of this clothing. This experiment suggests that any efforts toward increasing the physical well-being and efficiency of the soldier shall be directed toward protecting him from the debilitating effects of heat and humidity. One effect quite aside from these factors is that upon the eyes. We see here the result of the sunlight in many distressing symptoms, but these are probably due to the light rather than to the chemical rays. Any protection afforded the eyes from the glare of the tropical sun deserves to be heartily welcomed.

In closing I wish again to acknowledge the valuable work done by Major C. C. Collins, Lieutenants G. L. McKinney, Hiram A. Philipps, and C. D. Cowles, Jr., Medical Corps, in supervising the details of this test. Credit is also due to Captain Henry J. Nichols, Medical Corps, for assistance in outlining the experiment, and to Captain James D. Fife, Medical Corps, who placed his photographic appliances at our disposal.

TREATMENT OF STRYCHNINE POISONING WITH CHLOROFORM.

By A. O. Shaklee.

(From the Department of Pharmacology, Philippine Medical School, Manila, P. I.)

An experimental study of the treatment of strychnine poisoning was begun by the author earlier in the present year under the direction of Dr. S. J. Meltzer in the laboratory of the Rockefeller Institute for Medical Research, New York City. Two communications have since been published[1] in which reports were given of the treatment with curarin and artificial respiration by the continuous intratracheal insufflation of air by the Meltzer-Auer method. Another paper will soon be published on the treatment with ether. It was found in these earlier investigations that the lives of nearly all, if not all, dogs poisoned with twice the fatal dose of strychnine administered intravenously can be saved by the proper application of either of these methods. In the treatment with curarine, a small dose of atropine and considerable quantities of Ringer's solution administered intravenously together with artificial respiration seemed to be essential to success. In that with ether, recovery could be secured with ether alone, but the course of treatment was shortened by the intravenous administration of Ringer's solution, and rendered more certain by an exact regulation of the dosage of ether by means of insufflation and a mixing valve[2] for mixing the ether vapor with air in definite and constant proportions. The treatment with curarine seemed to demand close and constant supervision, while that with ether required comparatively little attention and caused no anxiety.

In the present investigation it is proposed to make a comparative study of the treatment of strychnine poisoning by means of ether and by means of chloroform. This seems desirable because of the fact that works on toxicology recommend the use of chloroform or ether without comment on their relative merits, or recommend chloroform without mentioning ether; and it seems important in view of what is already known of their relative toxicities to have some definite experimental results upon which to base the treatment of convulsions by the use of general anæsthetics.

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[1] *Proc. Soc. Exp. Biol. & Med.* (1910), 7, 96–97; *Berl. klin. Wchnsch.* (1910), **39**, 1776–1778.

[2] *Proc. Soc. Exp. Biol. & Med.* (1910), 7, 158–160.

The *method* of the present study in its main features is as follows: The preparation of the animal (1) for intratracheal insufflation with air mixed by means of the anæsthetic regulator[3] with the vapor of the anæsthetic; and (2) for intravenous injection of drugs and of Ringer-Locke solution warmed to the body temperature. In some cases a preliminary small dose of morphine, or atropine, or both is given. Since the non-anæsthetized animal which has not been treated with curarine, is thrown at once into a violent tetanic convulsion by the intravenous injection of strychnine sulphate in the dosage used, and since the spasm of the respiratory muscles may render the introduction of the anæsthetic difficult and hazardous, an attempt is made to bring the animal to such a stage of anæsthesia before the administration of the strychnine that no convulsions or only slight ones would result. At times the anæsthetic is administered by means of insufflation in connection with the anæsthetic regulator, at other times it is automatically administered by the dog's inspiration, the tracheal catheter being in connection with the regulator. The amount of Ringer-Locke solution injected in each case is equivalent to about one-tenth of the body weight and the duration of the injection varies from one-half hour to two hours. The quantity of strychnine administered varied from 0.6 to 0.8 milligram per kilogram of animal. In control experiments 0.4 milligram per kilogram proved invariably fatal to the untreated animal. When morphine or atropine is used, the quantity of morphine is sufficient to produce more or less depression and that of atropine large enough to liberate the heart from vagus inhibition.

The two protocols given below will show the course of the more successful cases of treatment with chloroform:

Protocol No. 4.—Dog No. 4, 12.5 kilos ♂, Brn. & Wh., 5 years old (?), seems healthy, rather lean.

8.25 a. m.: 1 cubic centimeter morphine sulphate (4 per cent aqueous solution) injected subcutaneously.

8.38: Pupils small.

8.45: Chloroform was administered by means of a cone. [In spite of care, an overdose of chloroform was given in this case and heart and respiration stopped. A tracheal catheter was inserted through the mouth and artificial respiration by insufflation together with thoracic (heart) massage were begun. The heart soon began to beat slowly but it was only after some minutes and after repeated strong traction on the tongue that voluntary respiration was initiated]. The tracheal catheter (a piece of rubber gas tubing) was connected with the anæsthetic regulator and valve set 4/6 full, i. e. was moved 4/6 of the part of a revolution necessary to send all the air through the anæsthetic bottle.

9.07: Chloroform 4/6 does not keep this dog under, owing to the excess in size of glottis over tracheal catheter. Pulse soft and irregular.

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[3] *Loc. cit.*

9.13: Chloroform 3/6 and trachea compressed closer to tracheal catheter by gentle outside pressure keeps the dog sufficiently anæsthetized for operation.

9.20: Pulse 66, full, fairly strong, drops a beat occasionally.

9.52: Pulse 60, full, strong, regular. Respiration 21, deep; expiration prolonged, and forcible. The pinching of the toe produces slight reflex. Pupils the size of pinhead.

9.56: Gently compressing trachea more closely on tracheal catheter increases percentage of chloroform sufficiently to abolish reflex from the pinching of the toe. Lid reflex sharp.

9.58: *0.83 cubic centimeter strychnine sulphate* (1 per cent aqueous solution) injected slowly into femoral vein along with Ringer-Locke solution.

9.59.5: Violent tetanus with rigidity of respiratory muscles and cessation of respiration. Thoracic massage and insufflation of dilute chloroform vapor maintained life and reduced the convulsion.

10.20: Chloroform 2/6+; voluntary movement; voluntary respiration; premonitory symptoms of convulsion.

10.21: Chloroform 4/6.

10.23: Chloroform 3/6—Ringer solution increased in rate.

10.27: Chloroform 3/6—Ringer solution increased in rate.

10.29: Chloroform 3/6—insufflation stopped. Compression of trachea onto catheter increases percentage of chloroform sufficiently to stop respiration.

10.35: Chloroform 2/6—insufflation.

10.45: Voluntary respiration weak. Ringer solution injection increased in rate.

11.02: Voluntary respiration fairly good. Lid reflex good. Rate of Ringer solution injection is about 20 cubic centimeters per minute.

11.45: The pinching of the toes causes slight reflex, but no symptoms of convulsions.

11.47: Injection of Ringer solution stopped. Total quantity injected=1,300 cubic centimeters.

11.50: Dog is hypersensitive—chloroform increased to 5/12.

11.55: Hypersensitive--chloroform increased to 6/12.

11.59: Chloroform reduced to 2/6.

12.04: Hypersensitive—choloroform increased to 3/6.

12.07: Compression of trachea removed.

12.10: Dog passes 2.5 cubic centimeters of very bloody urine.

12.26: Chloroform 2/6. Eyes closed.

12.28: Chloroform turned off. Dog breathes strongly and remains quiet.

1.10: Fairly strong clonic convulsions begin. They are brief and separated by intervals of only a few seconds during which the respiration is labored. Noises increase the strength of convulsions or bring them on. The convulsions are not so violent as to demand treatment.

2.20: Convulsions have practically ceased, 500 cubic centimeters of urine of nearly normal color passed. Respiration about 230 per minute and shallow with frequent short pauses.

2.26: Attempts to get onto feet.

2.40: Still hypersensitive.

2.45: Rose on his fore feet and stood for a time, but then failed in attempt to rise on his hind feet.

2.47: Rose on all four feet; legs very stiff, mild tetanic dance.

3.00: Able to walk fairly well, but staggers; lack of control is most marked in hind legs. Considerable exophthalmos.

4.30: Lying quietly; eyes closed; breathing 24 per minute, quiet, regular, practically normal. Pulse 60, full, strong, slightly irregular. Starts when disturbed. Refused drink.

On the next day the dog seemed in full possession of its faculties, but somewhat stupid or listless. On the third day the dog ate and drank, but was still stupid. Later on it began to decline and on the seventh day died. The gross appearance of the organs after death was not strikingly abnormal, but the lungs, heart and kidney seemed congested. A microscopic study of the organs will be made later.

Protocol No. 8.—Dog, 9.1 kilos, ♀, Brown native, lean, probably 5 years old, mangy.

1.25: 1 cubic centimeter morphine sulphate (4 per cent) subcutaneously.

2.00: 0.5 cubic centimeter atropine sulphate (1 per cent) intravenously.

2.05: Chloroform 2/6 with insufflation.

2.11: Chloroform 5/12, pulse 140 soft, marked venous pulse in neck, respiration 40, moderately deep, slightly irregular.

2.17: Pulse 156, respiration 48, shallow, irregular.

2.19: *0.73 cubic centimeter strychnine sulphate* (1 per cent) injected with Ringer-Locke solution, the injection of the latter solution was continued.

2.20: Strong tetanus, chloroform 3/6 with insufflation.

2.21: Eyes open and pupils wide. No convulsions, but limbs held in extension. Respiration shallow.

2.23: No lid reflex. Slight rythmic movement of hind legs.

2.31: Chloroform 5/12 with insufflation. No lid reflex. Respiration 42, deep, fairly regular.

2.37: Lid reflex fairly good. Chloroform 3/6 with insufflation.

2.39.5: No lid reflex, chloroform 5/12 with insufflation.

2.44: Slight lid reflex, foreleg still in extension and hind leg still in rythmic motion.

2.55: Chloroform 2/6 with insufflation.

2.59: Lid reflex good, respiration good, rythmic movements of fore legs, pulse 168, small, moderately strong, regular.

3.13: Fore leg relaxing.

3.24: Hypersensitive, lid reflex sharp, heart and respiration in good condition.

3.39: Sudden start, chloroform increased to nearly 5/12 with insufflation.

3.44: Injection of Ringer-Locke solution stopped, 900 cubic centimeters in all.

3.55: Chloroform 2/6.

4.01: Chloroform and insufflation off.

5.00: The dog has gradually recovered from the chloroform and is now attempting to rise to its feet.

On the following day the dog seemed normal, bright and strong; but the third day at 8.15 a. m. he began to droop and at 9 a. m. died quietly, about forty-eight hours after the beginning of the experiment. At autopsy the heart and liver were found very pale and yellow, suggesting marked fatty degeneration. The same appearances were found at other autopsies.

Results.—Of the first ten dogs of this series, one was given a small dose of curarine followed later by ether. This was the only one of the series that made a permanent recovery, in spite of the fact that the treatment was carried out by third-year medical students without previous experience in treatment of strychnine poisoning. The remaining nine dogs were treated with chloroform. Some had morphine as a preliminary, some had both morphine and atropine, and some had neither. Four of these dogs were saved from strychnine death but, these four died subsequently, apparently from chloroform poisoning. Two of the four had a small dose of morphine each, as a preliminary; one had morphine and atropine, and the fourth had neither.

Discussion.—A comparison of these nine cases treated with chloroform with the series of eleven treated with ether by the writer at the Rockefeller Institute, brings out a marked difference in the results of the two methods. Of the eleven dogs treated with ether only one failed to make a permanent recovery, and to that one the anæsthetic was administered by means of a cone provided with a wad of cotton soaked with ether. But of the nine treated here with chloroform none made a permanent recovery. At present it hardly seems possible to improve upon the treatment with chloroform as exemplified in protocol number 8,* to a degree that will remove the danger of subsequent chloroform death.

CONCLUSIONS.

1. Dogs poisoned with doses of strychnine which are certainly fatal may recover from the effects of the strychnine if properly treated with chloroform together with the intravenous injection of liberal quantities of Ringer-Locke solution.

2. Better results are obtained if the chloroform is given by intratracheal insufflation and in uniform concentration as low as consistent with the condition of the patient.

3. Dogs saved from strychnine death by means of chloroform are likely to die later of chloroform poisoning.

4. Chloroform is far inferior to ether for the treatment of strychnine poisoning, and probably for the treatment of convulsions in general.

5. Further experiment is necessary to determine the merits or demerits of atropine and of morphine in the treatment with chloroform of strychnine poisoning.

THE BONE LESIONS OF SMALLPOX.

By W. E. Musgrave and A. G. Sison.

(*From the Department of Clinical Medicine, Philippine Medical School, Manila, P. I.*

Eight patients have been admitted to our service during the past year, who were suffering from deformities of the forearms and hands caused by smallpox contracted during childhood. The following brief abstracts of that part of the records of these patients which bears upon the subject under consideration, together with photographic illustrations showing the deformities in six of the cases are submitted. We are unable to give radiograms because there is no satisfactory Röentgen apparatus at present available in Manila.[1]

Case I (*Plate I, figures 1 and 2*).—A. P., Filipina, 30 years old, born in Orani, Bataan, housekeeper, married, was admitted to St. Paul's Hospital July 27, 1910, because of labor and was delivered of a normal child on July 27, 1910.

The patient had a marked deformity of both forearms and hands which she states had followed an attack of smallpox contracted when she was about two years of age. The deformity (see figures 1 and 2) consists of a shortening of both forearms together with enlargement and irregular development about the elbow joints and irregular enlargements, shortening and other deformities of the bones of the wrist, hands, and fingers. The musculature, circulation and nerve supply in the deformed areas appear normal, except that there is some irregularity in the course of the vessels and the function of the forearms and hands is awkward and not complete, due to the abnormal relations about the joints and to the very definite shortening of the long bones. There are no subjective symptoms of any kind which may be associated with the lesions and there are no scars, contractions nor other evidences of an objective character or in the history which would indicate that the process was the result of an acute inflammation such as is sometimes seen about the joints in smallpox.

Case II (*Plate II, figure 1*).—B. P., Filipina, 19 years old, born in Orani, Province of Bataan, housekeeper, married, was admitted to St. Paul's Hospital July 25, 1910, because of labor and was delivered of a normal child on July 31, 1910.

The patient gave a history of smallpox at the age of 8 years, as a result of which she developed deformities in both forearms consisting of shortening of the radius and the ulna. The shortening is more marked in the left forearm than in the right. The articular surfaces in the elbow joint and in the wrist joint of the ulna and the radius are enlarged and irregular. Motion in these joints is fair in every direction, and there are no signs of abnormal limitation of movements. Musculature in good condition.

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[1] Such an apparatus has arrived and is now installed in the new Philippine General Hospital. (Editor.)

Case III (Plate II, figure 2).—V. P., Filipino, 33 years old, single, born in Santa Cruz, Province of Marinduque, was admitted to St. Paul's Hospital on August 22, 1909, because of chronic gastritis and was readmitted to the same Hospital for the same trouble on November 11, 1909.

When 8 years old, the patient had smallpox. The attack was followed by deformity and shortening of the ulna and the radius in both forearms, more pronounced in the left arm. Changes in the articular surfaces of the bones are the same as those described in the above cases. No deformity in the bones of the hands and fingers.

Case IV (Plate III, figures 1 and 2).—N. D., Filipino, about 25 years old, single, born in Santo Tomas, Province of Union. He came to the Free Dispensary complaining of beriberi.

When 5 years of age, the patient had smallpox which was followed by deformity and shortening in the bones of the forearms, more in the left than in the right forearm. No bone changes in the hands and fingers. Joints apparently not involved.

Case V (Plate IV, figure 1).—N. de la C., female, Filipina, 7 years old, born in Manila. History of smallpox at 3 years of age which was complicated by bone and joint lesions; the complications at present consist of bony ankylosis of the left elbow joint with distortion of the joint due to irregularities in the bones; apparent shortening of its ligaments about the right elbow and an enlargement of the end of the radius which gives deformity of the joint.

Case VI (Plate IV, figure 2).—P. S., male Filipino, 58 years old, born in Manila. History of smallpox at the age of 7 years, complicated by bone and joint lesions. At the present time deformity consists of shortening of both humeri, deformity of the left wrist with shortening of the ulna.

Cases V and VI both show extensive smallpox pitting over the principal areas of deformity.

Two other cases with histories similar to the above have failed to report to be photographed. Lesions similar to those described in the other cases were present in these patients.

DISCUSSION.

We have been unable to find in the literature of smallpox any mention of lesions similar to those here described. A condition involving changes in the bone marrow is recognized in a considerable percentage of cases of smallpox, and acute suppuration and other forms of acute arthritis occasionally are encountered in the disease. Paraplegia, due to lesions in the cord, are reported, and Osler mentions that "inflammatory process may occur in the bones."

However, none of these conditions are at all comparable to the findings in our cases, and for this reason it is necessary to elucidate two questions. (*a*) Are the deformities caused by smallpox? (*b*) If so, what is the nature of the lesion and what is its exact etiology?

The considerable number of cases with a similar history of smallpox during infancy and childhood followed by gradual development of the deformities, and in the absence of any other apparent cause, makes it fairly certain that the condition is caused by smallpox. Additional evidence of some value is found in the popular recognition of the condition as one of the complications of variola to such an extent that it is one of the occurrences most dreaded by mothers when they find that their children are suffering from the disease. The nature of the lesions could better be determined by the use of radiographs or by autopsies.

However, from the nature of the deformities and as a result of physical examination, the process appears to be due to destructive lesions in the epiphyses of the bones. The shafts of the ulna and radius seem to be normal, except in length. The ends of the bones are enlarged and irregular in shape and similar changes may be encountered in the carpal, metacarpal and phalangeal bones.

One of the most striking features of the deformities is the constant location of the lesions in the upper extremities, they usually being confined to one or both forearms, although they occasionally extend to the hands, as is shown in the illustrations.

The reason for not studying our cases with the X ray has already been given, and up to the present time we have not been able to examine any individual postmortem. However, in spite of the absence of radiographic pictures of the bones in question, it may be determined with considerable accuracy that the probable seat of the primary lesion which has prevented the further longitudinal growth of the bones is produced by the nature of the gross anatomical changes in the bone itself. To begin with, we have the following facts on which to base our argument

I. The circumferential growth of these bones is not disturbed in the least. There is no sign of underdevelopment in diameter, as can be proved by comparing them with normal bones. This shows that the periosteum upon which the circumferential growth depends, was not affected.

II. The bones are markedly shortened and stunted in longitudina growth, in some instances they are reduced to more than one-half th length of the normal bone.

The obvious conclusion from this fact is that the seat of the primary lesions is in that active part of the bone between the epiphysis and diaphysis which grows *ex utero.* This center of ossification consist of cartilage cells, upon which the longitudinal growth depends and which do not become calcified or ossified until late in life. Complet ossification of the ulna takes place from the twentieth to the twenty third year; of the radius from the twentieth to the twenty-fifth year and of the metacarpal and phalangeal bones at about the twentieth year At the the end of these periods of time, the diaphyses and epiphyses become firmly united and longitudinal growth ceases.

Is it not logical to reason *a posteriori* that the most probable cause of the deformity is primary inflammation and destruction of the secondary center of ossification situated between the epiphyses and diaphyses, resulting in premature ossification?

Another possible explanation of the deformity is that metabolic disturbances in the epiphysial cartilages have been induced by variola without primary, destructive lesions appearing in the cartilage itself. However, such a conclusion is hardly tenable if we remember that the articular cartilages of the affected bones show positive signs of irregular enlargement, bearing on them evidences of the ravages of a preëxisting inflammatory process underlying the whole trouble.

The special predisposition of the bones of the forearms and hands to this complication remains as the most difficult fact to explain. So far as we have been able to obesrve, the change does not occur in bones other than those which have already been mentioned; and such a complication is always seen in infancy and childhood during the period of active growth of the bones.

Additional note.—We have mentioned the shortening of the bones of the forearms, and also deformities in their articular surfaces; and while our article was in the press two more cases of bone lesion in smallpox of different character from those already mentioned came to our notice, the pictures of which are here respresented. One is that of a girl (see Plate IV, figure 1) about 9 years of age, who contracted smallpox when she was about 3 years old. As a result of the disease, she developed complete ankylosis of the right elbow-joint and partial of the left. Whether the ankylosis is bony or fibrous in character is difficult to say, though there are reasons for believing that the ankylosis in the right elbow-joint is of a bony character, as it is not possible to elicit the slightest motion in any direction, while that of the left is evidently produced by shortening of the particular ligaments of the elbow-joint.

The other case is that of a man (see Plate IV, figure 2) about 50 years old who contracted smallpox at the age of about 7 years, with a resulting complication of shortening of both humeral bones.

ILLUSTRATIONS.

PLATE I.

FIGS. 1 and 2. Case I. Showing marked deformity of both forearms and hands.

PLATE II.

FIG. 1. Case II. Showing shortening of ulna and radius in left forearm and deformity of right hand.

2. Case III. Showing shortening of both right and left forearms.

PLATE III.

FIGS. 1 and 2. Case IV. Showing deformity of both right and left forearms, more of left than right.

PLATE IV.

FIG. 1. Case V. Showing bony ankylosis of the left elbow joint with distortion of the joint.

2. Case VI. Showing deformity of both right and left forearms and of left wrist.

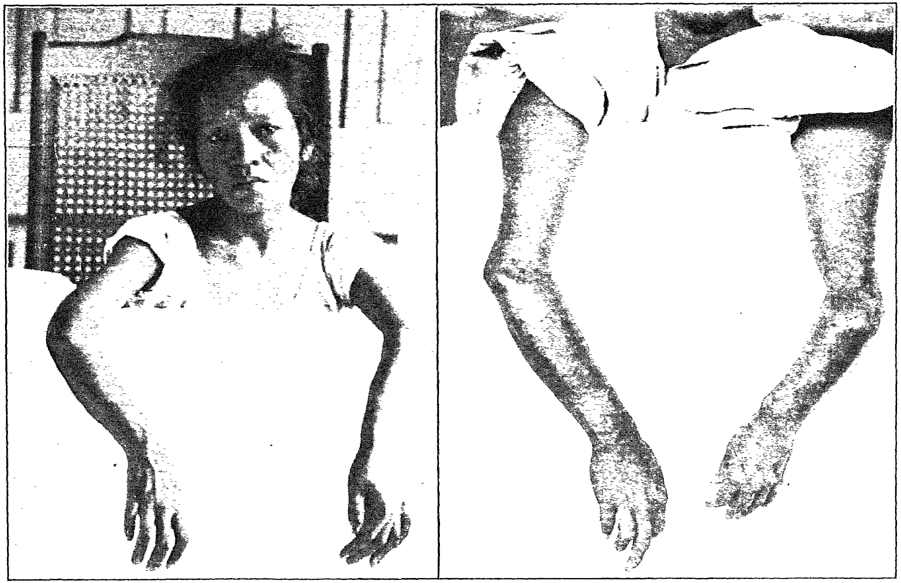

PLATE I.

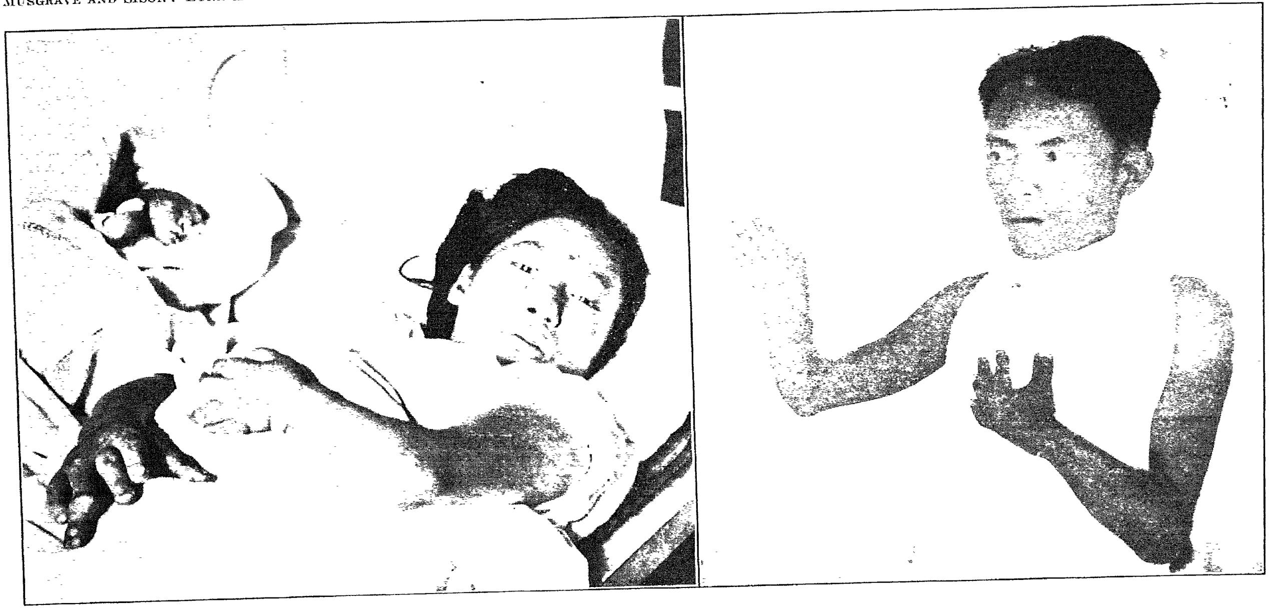

PLATE II.

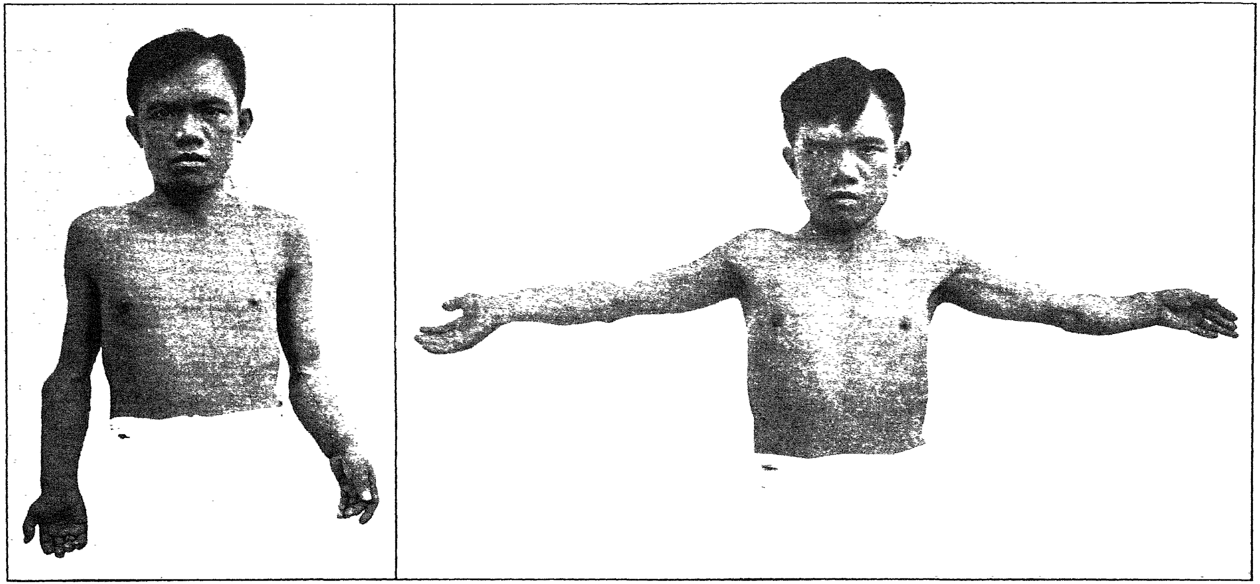

PLATE III.

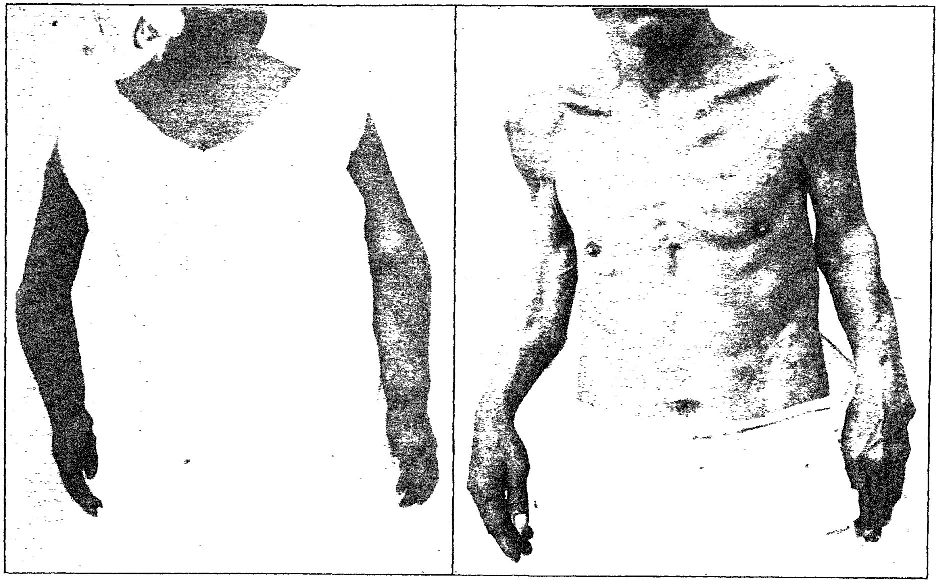

PLATE IV.

THE SPECIFIC TREATMENT OF LEPROSY.

By Eugene R. Whitmore[1] and Moses T. Clegg.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

Some months ago one of us[2] reported that he had cultivated an acid-fast bacillus from the spleen and from nodules from the ear in eight out of ten cases of leprosy. The procedure was to secure an amœba and a bacillus growing well in symbiosis and then inoculate the leprous tissue into this culture. The acid-fast bacillus was found to multiply in and around the amœbæ, while controls from leprous tissue without amœbæ and from normal tissue with amœbæ never gave a growth of an acid-fast bacillus. Clegg was able to transplant this acid-fast bacillus with the amœbæ and after repeating this operation for several months, he heated the tubes containing the cultures to 60° C for one-half hour and then allowed them to stand. After a few days, isolated colonies appeared on the tubes, and when transplanted they grew well on all media. These colonies proved to be pure cultures of this acid-fast organism, which we believe to be the leprosy bacillus.

The next step was the endeavor to utilize this bacillus in the treatment of leprosy. A vaccine was made in the ordinary way and standardized to five hundred thousand bacteria per cubic centimeter. The bacteria in this vaccine showed a great tendency to form clumps on being allowed to stand without shaking. We selected a number of well-marked cases of leprosy, all being positive for the leprosy bacillus. Injections were given once a week, the dose varying from 0.25 to 1 cubic centimeter. Several of the patients after the injections had local reactions in the leprous lesions, such as redness and swelling, and some pemphigoid eruptions; while two of the cases showed an extensive eruption of papules which were very red and tender. As the various eruptions disappeared, the skin remained pigmented at the site of the eruption. Upon increasing the dose of our vaccine we found that the dead bacteria were not absorbed, but remained at the site of the injection, and finally a small abscess would form and discharge a sero-purulent material.

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[1] Major, Medical Corps, U. S. Army; detailed to Biological Laboratory, Bureau of Science, Manila.

[2] Clegg, *This Journal, Sec. B* (1909), 4, 403.

Eleven cases of leprosy were treated with this vaccine for eight months, and twenty-one for seven months. At the end of the treatment there was no evidence of improvement in the condition of any of the cases, and, as we observed the formation of abscesses as soon as we increased the dose, it was decided to change to some other preparation.

We next employed a glycerine extract made from our acid-fast bacillus in the same way that old tuberculin is obtained from the tubercle bacillus. We tried the extract on leprous, tuberculous, and normal persons in the manner of the von Pirquet skin test for tuberculosis. Not one of the persons showed any reaction to the material.

We gave all the cases of leprosy in our vaccine series injections of this extract once a week, increasing the dose until 10 milligrams were administered at a dose at the end of two months. None of the patients had improved and no reactions had followed the injections.

Our next preparation was an emulsion of our acid-fast bacillus in a 1 to 60 aqueous solution of sodium oleate. The cultures on glycerine agar were scraped off and emulsified in the soap solution, so that one cubic centimeter of the solution would contain one milligram of moist bacteria. This emulsion was placed in the shaking machine for three days and then heated to 60° for one hour. The bacteria were nearly dissolved, there being only a slight sediment on allowing the solution to stand. When the preparation was shaken, the sediment was distributed freely through the solution without any tendency to form clumps. This preparation was sterile and remained so without the addition of any other preservative.

All the leprosy cases in our vaccine series were given injections of this new vaccine once a week. The dose was gradually increased until the patients were receiving one cubic centimeter of the emulsion, representing one milligram of moist bacterial substance, at a dose. Two cases developed a sharp reaction, with fever and malaise. There was considerable swelling and redness around the leprous lesions, especially on the face, hands, and feet. In no case was there local reaction at the site of injection, and no abscesses were observed. At the end of two and one-half months there was no improvement in the condition of any of the patients.

We next employed the spleens of patients dead of leprosy. We chose a spleen that was shown microscopically to be very rich in leprosy bacilli. We ground up this tissue and added a 1 to 60 aqueous solution of sodium oleate, so that one cubic centimeter of the resulting mixture would represent 0.5 gram of spleen substance. This mixture was shaken in the shaking machine for three days, filtered through cotton, and heated to 60° C for one hour. On standing, a small amount of sediment collected at the bottom, leaving the supernatant fluid clear and yellowish in color. This clear fluid was used for the injections. It was sterile and remained so without the addition of any other preservative.

All of the leprosy cases in our vaccine series were given injections of this preparation once a week. The dose was gradually increased until the patients were being given one cubic centimeter of the solution, representing 0.5 gram of leprous spleen tissue, at each injection. The cases have been receiving injections of this preparation for two and one-half months. None of them show any improvement in their condition and none of them have had any reaction after the injections.

When we started our vaccine work we put three cases of leprosy on weekly injections of atoxyl, and three on weekly injections of a mixture of sodium cinnamate and mercuric cinnamate. Injections were continued in these cases for eight months. None of the patients improved and none had reactions after the injections. We put our three "cinnamate" cases on injections of sodium cinnamate and a glycerine extract of our acid-fast bacillus, but at the end of three months there was no improvement and we discontinued the method of treatment.

Deycke injected cinnamic acid in order to produce a leucocytosis, and observed a greater reaction from Nastin in conjunction with cinnamic acid than from Nastin alone, but otherwise there was no result following the cinnamic acid injections.

At the time we began the specific treatment of our series of cases of leprosy, for nine months Doctor Teague[3] of this laboratory had been treating six cases of leprosy with injections of Nastin. He turned these patients over to us and we further treated them with the same injections for eight months. Every seven days each individual was given an injection of one cubic centimeter of Nastin B. At the end of eight months there was no improvement in the condition of any of the patients and none had any reaction after the injections.

SUMMARY.

1. We have prepared a vaccine, a glycerine extract and a soap solution, from an acid-fast bacillus which Clegg cultivated from leprous tissue. We have used these preparations in the treatment of cases of leprosy for twelve and one-half months, without noting any improvement in the condition of any of the patients. In some of the cases we have noted reactions after the injections, but we are not prepared to say whether or not these reactions are specific.

2. Our glycerine extract of this organism does not produce a skin reaction on leprous or tuberculous patients, nor on normal persons.

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[3] *This Journal, Sec. B* (1909), 4, 329.

3. We have treated these same leprous patients for two and one-half months with a soap solution of leprous spleen, rich in leprosy bacilli, without noting any improvement in the condition of the patients.

4. We have treated cases of leprosy for eight months with injections of atoxyl and also with injections of a mixture of sodium cinnamate and mercury cinnamate, without noting any improvement in the patients.

5. We have treated cases of leprosy for eight months with injections of Nastin B. These patients already had been treated with injections of Nastin B for nine months by Doctor Teague. At the end of the seventeen months, no improvement was noted.

TUBERCULOSIS IN THE PHILIPPINES: FINAL RESULT OF ONE YEAR'S SPECIFIC TREATMENT OF EIGHTY CASES OF PULMONARY TUBERCULOSIS.

By EUGENE R. WHITMORE.[1]

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

In January, 1909, I selected one hundred cases of pulmonary tuberculosis in the hospital at Bilibid Prison and divided them into five series for the purpose of testing several "specifics" in their treatment.

In August, 1909, I gave the conditions governing the selection of the series, and also reported the result of the treatment at the end of six months.[2] At that time I stated that at a later date I would publish a final report. The treatment was continued for one year, and the table below gives the result compared with a control series.

Series.	Died.		Returned to duty.		Remaining in hospital.		Released.
	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	
1. Tuberculin:							
A. By mouth	2	20	[a] 3	30 or 20	3	30	2
B. Hypodermically	4	40	3	30	3	30	0
Total for tuberculin series	6	30	[a] 6	30 or 25	6	30	2
2. Succinimide of mercury	9	45	3	15	7	35	1
3. Atoxyl	9	45	2	10	6	30	[b] 3
4. Cinnamate of mercury	4	20	7	35	8	40	1
5. Control series	4	20	4	20	9	45	3
Total	32	32	[a] 22	22 or 21	36	36	10

[a] One case returned to the hospital two months after his discharge, with an active pulmonary tuberculosis.

[b] One of the cases in the atoxyl series had gained 38 pounds in 35 days before his release.

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[1] Major, Medical Corps, U. S. Army; detailed to the Biological Laboratory, Bureau of Science, Manila.

[2] *This Journal, Sec. B* (1909), 4, 453.

The tuberculins used were "new tuberculin (T. R.)" and "old tuberculin (T. O.)" They were mixed and the dose at the beginning was $\frac{1}{1000}$ milligram T. R. and $\frac{1}{5000}$ milligram T. O. This dose was gradually increased until the patients took $\frac{1}{100}$ milligram T. R. and $\frac{1}{500}$ milligram T. O.

The patients in the "succinimide of mercury series" received injections of 13 milligrams or succinimide of mercury every other day for fifteen doses; then 26 milligrams every four days for fifteen doses; and then 39 milligrams once a week.

These of the "atoxyl series" received injections of atoxyl, soamin, or arsacetin: 65 milligrams every other day for fifteen doses, then 130 milligrams every four days for fifteen doses; and then 200 milligrams once a week.

The patients of the "cinnamate of mercury series" received injections of 18 milligrams of cinnamate of mercury every other day for fifteen doses; then 36 milligrams every four days for fifteen doses; and then 54 milligrams once a week.

The members of the control series received routine hospital treatment.

The cases taking succinimide of mercury and cinnamate of mercury experienced some trouble with sore mouths, especially in the early weeks of the treatment and the dosage frequently was cut down. Later, they bore the increased amounts better.

In all the series the dosage given above was used merely as a guide and was deviated from in individual cases as seemed advisable.

The treatment of all the cases was continued from January 14, 1909, to February 12, 1910, and the table gives the results up to the latter date.

CONCLUSION.

While the series is small and one must be very careful in drawing conclusions, still the result of this year's work seems to indicate that none of the "specifics" used by me were of especial value in the treatment of pulmonary tuberculosis in natives of the Philippines.

FURTHER OBSERVATIONS ON THERAPEUTIC INOCULATIONS OF BACTERIAL VACCINES.[1]

By EUGENE R. WHITMORE.[2]

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

At the annual meeting of the Manila Medical Society in February, 1908, I made some observations on the therapeutic inoculation of bacterial vaccines and it is my purpose now to add new points that I have gathered in the past year. The field of bacterial vaccination is too well known to require any general discussion of the subject.

One of the points which I emphasized was that it was not necessary to take the opsonic index regularly in order to control dosage, but that the clinical course of most diseases was a sufficient indicator. We all know that everywhere this is now the accepted idea and very few men are depending on the opsonic index for their indications for treatment. I also spoke of bacterial vaccination in gonococcus infections, and it is worth while to state my further experience in these infections. I do not see that in acute urethritis the vaccination in any way shortens the course of the infection, but I am of the opinion that it lessens the complications. However, it is difficult to say which cases would and which would not have complications under other treatment, and I know that bacterial inoculation does not entirely prevent complications, as I have seen an epididymitis develop in a case of urethritis that was being treated with vaccine.

In chronic urethritis the use of a stock gonococcus vaccine does not offer much hope. The infection here is usually mixed and it is necessary to make a vaccine from cultures obtained from the urethral discharge, or from prostatic milkings.

I have had several cases of from four to eight years' standing clear up in less than a month under treatment with a mixed vaccine and prostatic massage. These cases at the present time have remained entirely well for over six months. Some have improved under this treatment, while still others have not improved. In epididymitis the symptoms are usually relieved within twenty-four to thirty-six hours.

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[1] Read in part before the Philippine Islands Medical Association at Manila, P. I., on February 23, 1909.

[2] Major, Medical Corps, U. S. Army; detailed to the Biological Laboratory, Bureau of Science, Manila.

I have had five cases of gonorrhœal conjunctivitis, all the diagnoses having been confirmed by finding the gonococcus in the discharge from the eye. Two of these (both natives) did not come back after the first injection, so nothing is known of the result. The other three cases cleared up promptly after injection and none have any opacity of the cornea. One of these cases was an infant, eleven days old. One man had gonorrhœal conjunctivitis for two days. When the eyelids were separated the pus welled out. Thirty-six hours after the first injection the discharge from the eye was watery, and he made a prompt recovery with no opacity of the cornea. Some days later his vision was still low, but there was no apparent cause for it. I have been unable since to discover whether his vision returned to normal or not.

Gonorrhœa in women has not yielded satisfactorily to injections with a stock gonococcus vaccine in my hands. In one series I treated 110 women between March 16, 1908, and July 17, 1908. These were cases of urethritis, endometritis and bartholinitis and in all cases the presence of the gonococcus was determined by microscopic examination of stained smears. Of the 110 women, 31 came under treatment twice and 16 three times. They received in all 623 injections of stock gonococcus vaccine. There seemed to be some lessening of discharge in a few cases, but there was no evident shortening of the length of time during which the gonococcus was found in the discharge, and recurrences seemed to be just as frequent in the cases that received injections as in those that were not injected. From my experience with chronic urethritis it seemed to me that it would be necessary to make a personal vaccine in the cases of endometritis, and recovery was prompt in four cases of long standing so treated. One woman had been unable to do any work for two or three months and had been in bed a large part of the time because of pain in the pelvic region. There was considerable induration of the pelvic tissues as felt through the vault of the vagina, and examination was very painful to the patient. A vaccine made from the cultures taken from the cervical discharge was injected in conjunction with a stock gonococcus vaccine. After two injections the induration had disappeared and the woman resumed her household duties, including the regular laundry work.

Another series of cases of gonorrhœa in the female was treated by making a personal vaccine for each case and injecting it in conjunction with a gonococcus vaccine. When possible I prepared a personal gonococcus vaccine, but this was feasible in only a very small number of cases. A vaccine was made from the other organisms grown from the cervix in each case and this was combined with a gonococcus vaccine—personal when possible, otherwise stock.

Between December 1, 1908, and June 1, 1909, 156 patients were treated, and were given 653 injections of combined personal and gonococcus (stock or personal) vaccine. The results from this series were not any better than were those from a stock gonococcus vaccine alone.

My results in gonorrhœal arthritis have been excellent. I have treated 18 cases and have reports of 12 more that were treated with vaccine sent out by me, in all of which recovery has been prompt and complete. I recently have learned of three cases in which the outcome has not been satisfactory: two showing only moderate improvement after several injections, and one showing no change after a single injection.

The results of bacterial vaccination in chronic suppurative otitis media have been very satisfactory. I have treated, or prepared the vaccine for treatment of 51 cases. Three of these could not be followed. In 37, the discharge stopped after from one to four injections of a personal vaccine. In 11, the discharge did not stop after a prolonged course of injection. In six the discharge recurred. In the case of one little girl, the discharge from the ear ceased after several injections. The otologist in charge of the case reported that, to judge from an examination of the ear he considered the inflammatory process at an end. However, the little girl developed a meningitis a few months later and died. At the autopsy the case proved to be purulent meningitis due to extension from necrotic bone in the affected ear. The auditory canal was clean, and there was little evidence of inflammation in the lining of the middle ear. A few of the cases are cited below.

One case, suppurative otitis media, right ear, for several years. Left ear, for two weeks; furunculosis, left external auditory canal. Vaccine made from the discharge from each ear and the two mixed. Two injections, with interval of one week. Complete recovery in both ears, and the ears remain well 6 months later.

Another case, suppurative otitis media, left ear, for two weeks. Discharge stopped four days after first injection and ear remains well six months later.

A third case, with a left otitis media that had recurred several times at intervals of some months, received a single injection of a personal vaccine and the discharge ceased the next day. The patient left the city, and I understood that the discharge began again some time later. As the first dose is always a small one, I would not expect recovery in a long standing case from a single injection.

A fourth case, of suppurative otitis media with furunculosis of the external auditory canal, cleared up slowly under a personal vaccine and finally the discharge stopped and the patient expressed herself as feeling much better in general health than she had been previously. However, the purulent discharge from the ear has since recurred.

I have had an opportunity to treat four cases of pyorrhœa alveolaris with personal vaccine. Two cleared up entirely after a few injections, while the other two showed no apparent improvement after long series of injections.

A few practical points on dosage, vaccines, and injections seem worthy of mention. In the more acute conditions it is not advisable or possible to give as large doses of vaccine as when the condition has become more chronic. Thus, a chronic gonorrhœal arthritis will stand without any reaction a dose of gonococcus vaccine that will cause fever and marked discomfort in a case of epididymitis or acute urethritis. It is advisable in acute conditions to give small doses at shorter intervals and thus assist the body cells in walling off a process that threatens to become general; for instance, small injections of a personal vaccine in a case of cellulitis will localize the condition so that we have an abscess to open instead of a case of septicæmia to treat.

It is important to inject near the seat of the infection and in such a position that the lymph flows from the site of injection through the area of infection. A case of gonorrhœal arthritis of the right knee had received two injections of gonococcus vaccine in the buttock without any apparent effect on the lesion. The patient was then given an injection of gonococcus vaccine into the right leg about six inches below the knee. On the next day the relief from the pain was marked, progress toward recovery was rapid, and the patient walked out of the hospital in two weeks after the injection.

It sometimes happens that a case does not respond to injection with a personal vaccine, or else the response is satisfactory for the first injection or two and then the patient remains stationary or gets worse. In such instances a new vaccine should be prepared from fresh cultures, and this vaccine will often give satisfactory results.

It is important to continue the use of other accepted methods of treatment in a case that is receiving bacterial inoculations, and the production of local hyperæmia is always to be combined with bacterial inoculation wherever it is possible to do so.

In conclusion, I would say that bacterial vaccination is to be considered as an important method of treatment for certain diseases; in fact, there are a few conditions in which the results are far better than from other methods of treatment that we now have, but it is not in any sense a "cure all." In some conditions it does no good, in others it is of relatively slight value, while even in the diseases where the results are the most satisfactory there are individual instances where there is little or no impovement. Possibly, with increasing knowledge and experience we may learn the reason for some of our failures, and with this may come the ability to use the method with even better results than we are obtaining at present.

DISCUSSION.[a]

DISCUSSION ON THE PAPER, "AN EXPERIMENT WITH ORANGE-RED UNDERWEAR," BY DR. J. M. PHALEN.

Dr. Aldo Castellani, professor of tropical medicine and lecturer on dermatology, Ceylon Medical College, Colombo, delegate from the Government of Ceylon.—Doctor Chalmers and myself have made some experimental researches on the subject in Ceylon. We have compared the results obtained by exposing some rabbits directly to the sun-rays and by protecting others by placing white, red, etc., cloths on the cages. Those protected by red cloth, or by cloth, white outside and red inside, survived the longest. We also had good result by using Doctor Sanborn's "solaro" cloth. However, I frankly admit that experiments on man as made by Doctor Phalen are of more practical importance than experiments on rabitts as carried out by Doctor Chalmers and myself.

Dr. W. P. Chamberlain, major, Medical Corps, U. S. Army, president of the United States Army Board for the Study of Tropical Diseases as They Occur in the Philippine Islands.—These experiments do not show that khaki cloth is as protective as orange-red against the chemical rays that affect the photographic plate.

Dr. Victor G. Heiser, Director of Health for the Philippine Islands, professor of hygiene, Philippine Medical School, Manila, P. I.—The data given in this paper are indeed interesting. As I understand it, these experiments were carried out with soldiers who wore khaki outer clothing and controls wearing the same clothing. Furthermore, if I undertand correctly, the author states that he has observed individuals who have been in the Tropics for six years or more and who wore khaki clothing continuously, and that in such persons the protected skin showed no pigmentation, from which he inferred that the tropical light was effectively excluded by khaki. If this is the cause, it would seem that in order to draw correct deductions, it would have been better to make these experiments with soldiers who wore white outer clothing and orange-red underwear and with controls who wore white outer clothing and white underwear, or that one regiment should have been dressed entirely in white and compared with a regiment that was dressed in khaki.

REVIEWS.

Naval Hygiene. By James Duncan Gatewood, M. D., instructor in naval hygiene, U. S. Navy, Medical School, Washington, medical inspector, U. S. Navy. Prepared by the direction of the Bureau of Medicine and Surgery, and published by permission of the Navy Department. Cloth. Pp. xiv–779. Eight colored plates and 105 other illustrations. Price $6 net. Philadelphia: P. Blakiston's Son & Co., 1910.

This book, which specializes upon marine hygiene, is the first that has been published in English in over twenty years. The discussion of the relative prevalence of diseases as they occur in the United States Navy is well arranged and many deductions may be made therefrom.

The method of ascertaining the full damage done to the service in any one year by a single disease is entirely new and affords an excellent opportunity for testing the healthfulness of the service. However, the value of the book is detracted from by many statements which are not properly supported by evidence: For instance, it is stated on page 59 that continued residence in the Tropics tends to physical degeneration, and that experience has shown that the Navy should avoid the Tropics during the objectionable months. No evidence whatever is given in support of this statement and as such it can be regarded only as the opinion of one individual. On page 132, no mention is made of disinfection as a measure against smallpox, whereas, in other parts of the book, disinfection for other diseases is described in great detail.

It is believed that subsequent editions of this work could be much improved by eliminating some of the purely elementary matter and also by inserting additional headlines. The text sometimes goes on unbroken for 50 pages and the index is not sufficiently comprehensive to overcome this defect. However, the book on the whole is a most valuable one and should be on the shelves of all students of naval hygiene.

Doctor Gatewood is to be congratulated upon having produced so excellent a work in a field in which the literature is so meager.

V. G. H.

A Manual of Toxicology. By Albert H. Brundage, Professor of Toxicology and Physiology in the Departments of Medicine, Marquette University. 7. ed., revised and profusely illustrated. Cloth. Pp. x+428. Price $2.50 net. New York: The Harrison Co., and London: Baillière, Tindall & Cox, 1910.

Laboratory Text-Book of Embryology. By Charles Sedgwick Minot. 2. ed. revised. Pp. 402, 262 illustrations, chiefly original. Cloth. Price $3.50 net. Philadelphia: P. Blakiston's Son & Co., 1910.

As the name indicates, this book is not a laboratory guide for embryology, but a text-book for the laboratory study of embryology. Its scope is somewhat extensive and the material contained in it is for the most part essentially of a text-book nature. It is divided into eight chapters as follows: Chapter I, "General considerations," devotes thirty-one pages to an introduction to embryology and its various fundamental aspects. This chapter sets forth considerations which are to be borne in mind in studying any phase of embryonic development and which no doubt are meant to give the student a broader and more scientific point of view before taking up the detailed study of embryology. Chapter II, "The early development of mammals," after taking up first the histology of the male and female sex cells and the maturation of the ovum, at once enters into the study of the embryonic development of mammals, the most difficult group we have in embryology. Chapter III, "The human embryo," deals with the different stages of development of the human embryo. Several good illustrations are given. Chapter IV takes up the "Study of the segmentation of the ovum and of the blastodermic vesicles in mammals." Chapter V devotes 45 pages to the "Special embryology of the chick and its relation to development in the mammals." Chapter VI, "Study of pig embryo" covers 120 pages and from the standpoint of strict embryology is perhaps the most valuable section of the book. The embryonic development of the pig is portrayed in a comprehensive and lucid manner and the many excellent drawings and reconstructions in this chapter make it easily understood, and give an excellent conception of the extent of development of the various organs and tissues and their relations to one another in the different stages of the embryonic history of this animal. Many of these illustrations are so clear, that they alone, with their explanatory descriptions, would give a pretty fair idea of the embryology of the pig. Chapter VII, "Study of the uterus and the fetal appendages of man," embraces a study of the histology of the uterus, menstruation, the pregnant uterus, decidua, chorion, amnion, placenta, etc. Several stages of some of these are taken up and illustrated. Chapter VIII, "Methods," gives several valuable suggestions in regard to preparing and measuring embryos and the preparation of sections of embryos.

The subject-matter is thoroughly reliable, excellent, and well correlated. However, the arrangement probably deserves severe criticism. While being an improvement over the former edition in that the study of the embryo begins at the early stages and leads up to the later, instead of the reverse, it still by no means conforms to the arrangement of subject-matter, which, by embryologists, usually is considered chronological.

The simpler forms, including the chick or the frog, are generally taken up first as they are supposed better to help us to understand the more complex forms, including man.

In reading the book through, the impression was gained that, with the above limitation, it is well suited for students of embryology who have had a well-grounded preliminary training or an introductory course in embryology, in institutions which possess a good embryological museum, a good technician, and a graduate staff of instructors. Elsewhere it well deserves a place in the library as a book of reference, but not as a laboratory text of embryology.

ELBERT CLARKE.

Medical Education in the United States and Canada. A Report to the Carnegie Foundation for the Advancement of Teaching. Bulletin No. 4. By Abraham Flexner. With an introduction by Henry S. Pritchett, President of the Foundation. Paper. Pp. XVII+346. 576 Fifth Avenue, New York, 1910.

No publication of the year 1910 has occasioned so much interested comment, and none will be the cause of so much general good to the community as this report to the Carnegie Foundation on Medical Education in the United States and Canada. If a Noble prize were to be awarded for the most stimulative and the most courageous publication of the year, Doctor Flexner should have first mention. It has required no minor quality of courage for the president of the Carnegie Institution and the author of the report to attack so boldly the evils of our medical educational system. Educational authorities are no less firmly intrenched behind the barriers of their self-esteem and the customs of the past than are the "malefactors of great wealth," and the principle upon which rest the people's campaign against unjust corporations and this newly organized war upon unfit educational institutions is the same, namely, that all institutions which fail to serve the people well and with undivided interest must make way for such as shall.

In regard to medical education, we are begining to realize the fact that those who pay the bill for the education of a physician are not those who furnished the modest amounts necessary to meet the registrar's fees, but the members of the community among whom the physician lives after receiving his license to practice the art of healing; and a costly education it proves for many a community which is plagued by an illy equipped, ignorant, unskillful doctor instead of being benefitted by the skillful physician it has the right to expect. Reading the pages of this report intensifies the horror most of us have of being obliged to call in a doctor of whom we know nothing except that he has the degree of M. D.

"The day has gone by when any university can retain the respect of educated men, or where it can fulfill its duty to education, by retaining a low-grade professional school for the sake of its own institutional completeness." [1]

For the purposes of the report, every medical school in the United States and Canada, of every sect, has been visited by the author. Doctor Flexner is not the first carefully to inspect the work and equipment of these schools, so every statement of his has been checked and corroborated. The essential part of the report is that which includes his statements of the equipment of each school. The States of the Union are taken up in alphabetical order. In each case the population of the State and the ratio of physicians to population are given. The report on each institution considers the entrance requirements, attendance, teaching staff, resources available for maintenance, laboratory and clinical facilities. These individual reports are succinct, accurate, and just. Where schools are honestly doing their best, although under a mistaken impression of their duty to the public, the author does not begrudge proper recognition of this spirit. For example, at the Woman's Medical College of Baltimore, with an attendance of 22, and resources from fees amounting to $2,000 a year, "small laboratories, scrupulously well kept, show a desire to do the best possible with meager resources." But, unfortunately, the majority of the medical schools of the United States are found to be doing anything but their best, and the conditions of these schools are described without mercy. Of one medical college the report says: "There is no outfit worth speaking of in any department; the building is wretchedly dirty, especially the room said to be used for anatomy. There is nothing to indicate recent dissecting * * *. There is no organized dispensary." It is a difficult, though interesting, task to discover which is the worst school among the many that are unfit to exist.

Of another college the report says:[2] "The school building is wretchedly dirty. Its so-called laboratories are of the worst existing type; one neglected and filthy room is set aside for bacteriology, pathology, and histology; a few dirty test-tubes stand around in pans and old cigar boxes. The chemical room is perhaps equal to the teaching of elementary chemistry. The dissecting room exhausts its teaching facilities. There is no museum or library and no teaching accessories of any sort whatsoever."

Of still another,[3] Doctor Flexner reports: Attendance 172; teaching staff, 30 professors and 15 lecturers; fees amounting to $10,000 per annum are its sole resources; a reduction of 20 per cent is made to students who pay in advance for the entire four years; laboratory facilities "are wretched; ill-lighted, dirty, and poorly equipped so-called laboratories are provided for anatomy, pathology, etc. The clinical facilities are dubious. The catalogue attempts to convey the idea that the school has the same opportunities as Harvard and Tufts; as a matter of fact no member of the faculty * * * has a staff appointment in the city hospital, and teaching there is utterly impossible otherwise. * * * A limited attendance is required at a miserable dispensary, more than an hour's journey from the college building."

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[1] Introduction to the Report, page XI.

[2] Page 237.

[3] Page 242.

There is no need to make a list of all the schools the resources of which are wholly from fees, and mostly diverted to stockholders pockets, or the laboratories of which are nil, or "hopelessly meager," "absurdly inadequate," "make-believe," "dirty," or "filthy," or whose clinical facilities are utterly inadequate. Suffice it to say that the good schools are very much in the minority, and yet there are a sufficient number of them to supply the country with all the doctors of medicine needed. The pity of it all is that almost every student at every low-grade medical school is earnestly desirous of a good education, is paying for it, and believes he is getting it. It is not until he has graduated that he learns that his education has been defective. How defective is vividly illustrated by the class of "post-graduate" schools which have sprung up in order to catch these very men under the guise of helping them to overcome their deficiencies. For example, notice the report on one post-graduate school of medicine. "A post-graduate institution organized as a stock company. Offers special courses to graduate physicians. Attendance: Perhaps 30 at any given time; a total of 350 in the course of a year. Teaching staff: 92, 30 being professors, 62 of other grade. Resources available for maintenance: Fees. Laboratory facilities: A small clinical laboratory, the instruction in technique being given by a first-year student in one of the night schools; in the absence of the instructor he also conducts classes. Clinical facilities: The main reliance is the hospital of the institution, of 80 beds, two-thirds of them surgical." Apparently the average post-graduate college has little real help to offer the physician.

The report does not attempt to give the histories of any institution, only what they are now. There is a general historical account of medical education in the United States, followed by a thorough discussion of the laboratory branches and the relations of the medical school to the hospital and dispensary. A chapter is devoted to the financial aspects of medical education, and finally the all-important subject of reconstruction is discussed. The plan proposed is admittedly theoretical, yet it is specific in that the favorable locations of the medical colleges of the future are pointed out. As long as medical schools are left to organize and reorganize as they please, to establish their own entrance and graduation standards, and to determine freely the amount of practical clinical work necessary, so long will many doctors seize the opportunity for advertisement and reputation which connection with the staff of any sort of a school affords and so long will poor schools remain with us. The ignorant student who will be attracted to these schools in spite of the presence of the really good schools, will always exist. But the establishment of standards of entrance and equipment to which all schools must conform will very soon eliminate the majority of American medical schools, and the probabilities are that the ideal plan of Doctor Flexner will very nearly be realized in a comparatively few years. The plea that young men must not be compelled to spend so many years in study that they will be well along in the twenties before commencing the practice of medicine is losing its force before the realization that a few years more of practice for the physician is a small matter compared with the welfare of the community.

Aside from its direct bearing on medical education, this report will have a far more widespread and important effect upon education in general. Every experienced educator knows that the "colleges" of the United States stand in more need of regulation and standardization than even the professional schools. The name of college covers a multitude of educational sins, and even many serious sins resulting from greed, envy, and cupidity, not to mention ignorance. We hope that the time is not far distant when a plain-spoken, brutally truthful account will be given of every college in the United States, which shall force each into its own proper position in the educational system. But as long as the reports on education consist of statistical tables of the faculties, equipment, and financial resources of the colleges (as the colleges themselves report them for publication) and perfectly harmless essays upon the systems of education in Germany, France, and England, there exists no basis for the establishment of college standards. The most efficient educational work to-day is being done by certain of the State universities of the Middle West in their supervision of the high schools.

LAWRENCE E. GRIFFIN.

An International System of Ophthalmic Practice. Edited by Walter L. Pyle, A. M., M. D. **Therapeutics**, by A. Darrier, M. D. Translated by Sydney Stephenson, M. B. Cloth. Pp. xxiv+444. Price $4.00 net. Philadelphia: P. Blakiston's Son & Co., 1910.

The relative value of a modern work on therapeutics can be discussed from many viewpoints. The editor of "An International System of Ophthalmic Practice," states in his preface that the purpose of this work is to present up-to-date methods of ophthalmic practice.

A recent method of cataract extraction as used by Smith, in India, is not mentioned. Favorable results with argyrol in maternity hospitals as a Credé substitute are stated, but no mention is made of the fact that several practitioners have abandoned its use as unreliable. Whether right or wrong, a one-sided statement is open to criticism.

The subject-matter is arranged under the headings "General therapeutics" and "Special therapeutics." Under "General therapeutics," the reviewer is impressed with the author's faith in the value of "paraspecific thereapy," "guaiacol," "subconjunctival injections," and the ease of obtaining accurate laboratory confirmation in the diagnosis of eye affections. A too general use of many remedies as specifics, when unsupported by reliable statistical data, has in the past resulted in losing sight of their true value. It has taken years for "tuberculin" to recover from such a doubt. Further, it is difficult to believe that one or two attempts are sufficient to make laboratory diagnoses easy of accomplishment. An accurate Wasserman's reaction is never a simple matter. The use of such an expression as "arthritism," meaning absolutely nothing, is objectionable.

The second part of the book, under the heading of special therapeutics, gives in detail pathologic conditions of the eye and its adnexa. The affections are grouped into separate chapters, beginning with diseases of the orbit, following through the various anatomical structures to the retina. There is little new in pathology, diagnosis or treatment, but special stress is laid on the great value of injections of mercury, intravenous or subconjunctival, paraspecific therapy, organic silver salts, and dionin.

The different nationalities engaged in presenting this book are in keeping with the international character of the system. The brief footnotes of the editor make the reader regret that he has not made more liberal use of his control. Such notes, stating that "correcting lenses in blepharitis marginalis is a sine quo non," and "the stimulation of compensatory accommodative power by any means is likely to be followed by all the baneful local and reflex symptoms of ametropic eyestrain," are excellent. Similar footnotes, condemning strongly such drugs as "atoxyl" and such a reaction as that of "Calmette," should have been made. Had chapters 7, 8, 9, and 10 been condensed into one, much that is of little value would have been eliminated.

As a reference book, "An International System of Ophthalmic Practice" can hardly be recommended, because of its looseness in grouping, and absence of a bibliography, but it shows advanced thought and gives an insight into the future lines of progress in ophthalmic practice.

T. C. LYSTER.

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